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DIE ALGEMENE PRAKTISYN: PROBLEME EN STANDPUNTE

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'Ons genees maar selde, ons verlig soms—ons troos egter altyd.'

—Sir William Osler.

Hierdie woorde het deur die jare 'n trotse erfenis en prestige verleen aan die huisdokter of die algemene praktisyn.

In Suid-Afrika is die algemene praktyk op 'n stewige fondament geplaas. En waar die geneeskundige praktyk tans sy kinderskoene ontgroei, word daar baie gegis oor die toekoms van die huisdokter. Die besluit is egter eenparig dat sy rol in die toekoms nog belangriker sal wees. 'n Besluit gesteun deur die kliniese spesialis, die navorser en die administrateur op die drie ander hoofrigtings van die geneeskunde.

Enkele probleme en standpunte van die huisdokter kan saamgevat word onder die volgende hoofde: (*a*) Sy rol in die verlede, (*b*) Sy rol in die hede, (*c*) Sy rol in die toekoms.

A. DIE ALGEMENE PRAKTISYN SE ROL IN DIE VERLEDE

Op die grootpad van die mediese geskiedenis is daar ook die bakens wat deur algemene praktisyns opgerig is. Die volgende drietal het, nieteenstaande beperkinge, skitterende mylpale bereik.

Sir James Mackenzie. As praktisyn in Burnley, Engeland, het hy hom aanvanklik veral op verloskunde toegelê. Maar die onverwagte dood van 'n jong vrou weens hartverswakking tydens kraam, het 'n verandering by hom teweeggebring. Hy het naamlik toe begin om 'n spesiale studie van die kardiovaskulêre simptome en tekens van sy pasiënte te maak. Dit was baanbrekerswerk wat die naam van hierdie beminde huisdokter vir altyd gekoppel het aan die kardiologie.

Dr. Edward Trudeau. Hierdie praktisyn moes weens longtuberkulose hom gaan vestig in die woude van die Adirondacks op die Amerikaanse vasteland. In 'n studie oor wat destyds bekend was omtrent die behandeling van tuberkulose, het hy 'n bydrae van Dettweiler teengekom. Laasgenoemde was die eerste om buitelugbehandeling, vergesel van rus, vir teringlyers te bepleit. Besield is Trudeau na New York om fondse in te samel. En in 1885 rig hy daarmee die eerste sanatorium op by die Saranac-meer 'n Grootse bydrae deur 'n algemene praktisyn om tuberkulose te verander in een van daardie siektes wat wel genees kan word.

Dr. Albert Schweitzer. Hierdie musikus-teoloog-filosoof-medikus van Lambaréne, in Sentraal-Afrika, het in ons dekade die bewys gelewer dat naastediens nog die hoofdoel van die geneeskunde is. Die volgende opskrif begroet die vreemdeling digby die hospitaal waar Albert Schweitzer die werk van 'n algemene praktisyn doen:

Op welke uur van die dag of nag u mag kom, sal u hier vind hulp, lig en menslike liefde.

Daar is dus 'n ryk verlede om op te bou vir hulle wat altyd in die algemene praktyk wil bly.

B. DIE ALGEMENE PRAKTISYN SE ROL IN DIE HEDE

Drie faktore beheer teenswoordig die rol van die huisdokter.

1. *Die Verhouding tot die Pasiënt.* Die huisdokter se werk is die toepassing van geneeskunde as 'n wetenskap en kuns in besondere omstandighede en met besondere hulpmiddels. Meestal behandel hy die pasiënt tuis, en die huisdokter tree ook op as raadgewer en vertroueling. Mettertyd mag hy die biegvader word van sy omgewing. Sir William Osler het hierdie roeping baie helder gestel:

'The practice of Medicine is an art, not a trade; a calling, not a business; a calling in which your heart will be exercised equally with your head.'

2. *Die Huisdokter as Wetenskaplike Medikus.* Die skynbare onmoontlikheid van dié stelling het bygedra daartoe dat baie medici die algemene praktyk nie as 'n permanente rigting kies nie. Daarom word die algemene praktyk soms beskou as slegs 'n tussenstadium vir die wordende kliniese spesialis. Die leke-publiek gebruik ook op die oomblik gespesialiseerde kennis as die maatstaf waarmee die moderne medikus se bekwaamheid gemeet word; en nie sonder rede nie. Elke algemene praktisyn sal erken dat op hierdie pad wat weglei vanaf die verligte voorlesingsaal, daar tog 'n bedreiging

is om deur die stowwe van die tyd toegewaai te word. Selfkritiek oor sy diagnostiek en metodiek van behandeling mag met die tyd verswak. Gelukkig is daar die rooidag van 'n nuwe môre aan die horison. In Brittanje is algemene praktisyns reeds besig om navorsing en wetenskaplike werk in die praktyk toe te pas. Die jongste nuusbrief van die ‚College of Practitioners' weerspieël nog onsekerheid oor die verskillende terreine wat betree sal kan word, maar dit lei 'n nuwe tydperk in. En die huisdokter of algemene praktisyn van die hede sal pionierswerk doen deur die terreine te vind waar navorsingswerk in die algemene praktyk gedoen kan word.

In ons land is die vraagstuk van tuberkulose van geneeskundige sowel as ekonomiese belang. *Die diagnose van tuberkulose op die platteland berus uitsluitlik by die algemene praktisyn.* Die stygende voorkomssyfer van tuberkulose onder nie-blankes in die binneland sal tuisbehandeling ook noodsaaklik maak. Juis dit sal die vroeë diagnose van die jong positiewe kontak so nodig maak.

Met staatshulp kan hierdie probleem omskep word in 'n navorsingsterrein van groot geneeskundige, ekonomiese en sosiale betekenis. En die algemene praktisyn kan hier 'n belangrike rol vervul.

3. *Probleme van Diagnose en Behandeling.* Die volgende geval sal as voorbeeld dien van hierdie aspek om veral 3 dinge te illustreer:

(*a*) Die ernstige siektebeelde moet onderskei kan word van die alledaagshede.

(*b*) Die behandeling van 'n siektebeeld sonder 'n vasgestelde diagnose.

(*c*) Die siektebeeld se verloop moet aan die familie van die pasiënt in hul eie taal verduidelik word.

Mnr. I. v. R., 73 jaar oud, 'n gesonde aktiewe boer, het op 10 Februarie 1954 om 8 nm. kouekoors ontwikkel met occipitale hoofpyn wat afgetrek het na die skouers. Daarby het hy 'n naerheid beskryf wat uit epigastrium tot in die keel opgestyg het. Egter geen kortasemheid, hartkloppings of vomering gehad nie. Vorige geskiedenis van longontsteking in 1937.

Ondersoek. Om 4 vm. op 11 Februarie is 'n skraal, ouerige pasiënt aangetref wat plat in die bed gelê het, en onrustig en ligsku voorgekom het. Temperatuur 98.6° F. Polsspoed 65 per minuut met gereelde ritme en volume goed. Bloeddruk 130/80 mm. Hg., wat ook die normale lesing was. Die pupille reageer eners. Daar was drukteerheid oor die nekspiere. Geen nekstyfheid, kongestiewe nekvenae, cyanose of edeem gevind nie. Beweging van borskas was simmetries. Die hart was nie vergroot nie en hartklanke sag en geslote. Enkele rhonchi by longbasisse gevind. Geen drukteerheid oor die buik nie en geen milt of lewer kon gevoel word nie. Die prostaat was nie vergroot nie. Die kraniële senuwees was normaal asook die ander reflekse van die senuweestelsel. Geen kliere kon gevoel word nie. Die urine het geen suiker of albumin bevat nie, en die volume was normaal.

'n Griepaanval gediagnoseer en behandeling was simptomaties. Omnopon gr. 1/3 ook toegedien.

Verloop. Op 11 Februarie om 7 nm. was die pasiënt se temperatuur 100.6° F., met die nausea sonder vomering nog die uitstaande simptoom. Bykomend was daar toe 'n onproduktiewe hoesie en 'n area van pleurale wrywing by regter longbasis is gevind. Penicillin 500,000 eenhede 6-uurliks toegedien.

Op 12 Februarie om 8 vm. was die temperatuur 101° F. met die pols, asemhaling en algemene voorkoms nog baie min verander sedert die aanvang van die siekte.

Verdere ondersoeke het op daardie tydstip die volgende aan die lig gebring: Witseltelling: 4,600 per c.mm. met normale indeling. sedimentasie: 20 mm. na 'n uur (Westergren).

Lumbaalpunksie: helder vog wat nie onder druk was nie. Die urine se volume het goed gebly met hoë konsentrasie.

Die oggend van 12 Februarie het ons dus 'n ouerige pasiënt gevind, voorheen gesond, wat, behalwe verhoogde temperatuur en rusteloosheid min ander simptome en tekens gehad het. 'n Bevredigende verklaring aan die bekommerde familie was moeilik om te maak. Die longtekens kon kwalik verantwoordelik gehou word vir die siektebeeld. Weens stygende temperatuur vanaf 2 nm. is Aureomycin toe ook per mond gegee.

Vanaf 5 nm. op 12 Februarie versluier sy geestestoestand. Die rusteloosheid het oorgegaan in delirium. Die polsspoed het die hoogte ingeskiet buite verhouding tot die verhoogde temperatuur. Konvulsies het die koma voorafgegaan wat toe ingetree het. Daarmee is 5% glukose in soutoplossing binne-aars gegee, en intussen suurstof onderhoudend.

Om 10 nm. het hy erg dispnea, gestude nekvenae en pulsasies oor praecordium ontwikkel. Gallopritme het ingetree. Cedilanid en aminophyllin gesamentlik binne-aars gegee. Cheyne-Stokes-asemhaling was egter reeds aanwesig en die pasiënt is om 11.30 nm. oorlede.

Differensiële Diagnose: 1. Patologie van die brein, hetsy bloeding, trombose, embolus of infeksie, wat nie 'n klassieke patroon gevolg het nie.

2. 'n Infarksie van die myocardium.

3. 'n Infektiewe proses vanuit die longe.

Die probleem om 'n diagnose te maak het dit verder bemoeilik om te besluit op prognose en behandeling.

So dien hierdie geval dan as slegs 'n voorbeeld om die huisdokter se probleem te skets, in diagnose en behandeling, veral op die verafgeleë plattelandse dorp.

C. DIE ALGEMENE PRAKTISYN SE ROL IN DIE TOEKOMS

Die organisasie van geneeskunde mag in die toekoms radikaal verander word. Maar een ding verseker die toekoms van hulle wat die algemene praktyk as 'n permanente rigting kies. Dit is dat die mens nog altyd eers na die huisdokter kom met die vae klagtes en weinige tekens van die ernstige patologie, wat nog in in behandelbare of geneesbare stadium is.

Toegewyde praktisyns weet dat hierin ook 'n uitdaging is en verlang daarom na die stimulus tot nagraadse studie wat die beoogde kolleges en praktisynsgroepe sal aanbied.

SAMEVATTING

1. Drie bekende persoonlikhede uit die professie geneem wat as algemene praktisyns blywende werk gelewer het.

2. Die huisdokter se rol in die hede geskets as wetenskaplike medikus.

3. Die toekoms se moontlikhede vir diegene wat sal voortgaan as algemene praktisyns.

SUMMARY

The author makes a plea for the status of the general, and more particularly the rural, practitioner as the most important member of the medical team. He illustrates his points by quoting from the past 3 examples of general-practitioner achievement, and from the present a case report to illustrate the isolated practitioner's difficulties; and he looks bravely and hopefully at the future.

VERWYSINGS

1. Coope, R. (1952): *The Quiet Art.* 1st. ed. p. 250. Edinburgh en Londen: E. & S. Livingstone, Ltd.
2. College of General Practitioners, Research Newsletter No. 2. *The Practitioner.* **172,** 1030.

South African Medical Journal

Suid-Afrikaanse Tydskrif vir Geneeskunde

VAN DIE REDAKSIE

SIMPOSIUM OOR VIRUSSIEKTES

Ons hervat ons bespreking van die simposium oor virussiektes[1] deur die *Practitioner* gereël, waarna ons onlangs verwys het[2] en waartoe verskeie uitstaande navorsers bygedra het.

In die inleidingsartikel van die simposium toon Van den Ende van Kaapstad dat die virus nou duideliker uitgebeeld is. Virusse is ultramikroskopies met relatief ingewikkelde chemiese bou wat hoofsaaklik uit proteïene en kernsuur bestaan. Aan die laasgenoemde bestanddeel kan hul spesifieke aktiwiteit waarskynlik toegeskryf word. Vir navorsers op baie gebiede, o.a. natuurkunde, biochemie, genetika en natuurlik bakteriologie, is virologie 'n jagtershemel. Navorsing in bakteriofage (*bacterium-bacteriophage* stelsel) het byvoorbeeld die proses van binne-sellulêre vermenigvuldiging van die virusse toegelig.

Die immunologiese probleem van griep is deur Andrewes bespreek wat onlangs lesings in Suid-Afrika[3] oor hierdie onderwerp gegee het. Die beheer van griep deur enting sal beteken dat miljoene mense elke ander jaar ingespuit moet word. Dit is twyfelagtig of dit vir gewone griep prakties sal wees. Die skrywer wys daarop dat die ontwikkeling van entstowwe hoofsaaklik nodig is om vir 'n dodelike pandemie, soos dié van 1918—19, die hoof te bied. Doeltreffende entstowwe teen griep kan vervaardig word maar hul lok onaangename reaksies uit en dit is moeilik om die waarde van die entstofproefresultate te bepaal; dit is veral te wyte aan die feit dat dit moeilik is om die siekte klinies te diagnoseer. Selfs 'n serologiese diagnose wemel met strikvalle en as die hele gemeenskap ge-ent is, is dié diagnose van minder waarde as gewoonlik. Dit is 'n gewigtige vraagstuk want as virusse gedurig veranderings ondergaan (aangesien hul antigenies nie stabiel is nie) volg dit dat nuwe entstowwe vervaardig moet word en hul immuniserende uitwerking mag varieer. Dit sal moeilik wees om 'n langdurige immuniteit te verkry. Andrewes doen aan die hand dat die mees effektiewe entstowwe opsy gesit word vir belangrike mense wat sleutelposisies beklee en vir ander wat daarvoor vra. Om entstowwe op groot skaal te vervaardig, wat veilig en doeltreffend is, neem betreklik lank en dit is 'n praktiese probleem waarmee rekening gehou moet word as enige poging om 'n epidemie of pandemie te beheer, oorweeg word.

Immunisasie teen poliomiëlitis het in die jongste tyd wye publisiteit ontvang en tot dusver kom dit voor asof redding teen die gevreesde siekte hoofsaaklik by immu-

EDITORIAL

THE VIRUS DISEASE SYMPOSIUM

We return to the *Practitioner's* symposium on virus diseases[1] to which we referred recently,[2] and which included contributions by several distinguished investigators.

In the introductory article to the symposium van den Ende, of Cape Town, shows how a clearer picture of the virus is emerging. Viruses are ultra-microscopic and to be regarded as relatively complex chemical structures in which the essential constituents are protein and nucleic acid. The latter substance probably gives them their specific activity. Virology is a happy hunting-ground for research workers from many fields, including physicists, biochemists, geneticists and of course bacteriologists. Research on bacteriophage (bacterium-bacteriophage system) has lead to the elucidation, for example, of the process of intracellular multiplication of viruses.

The immunological problem of influenza is discussed by Andrewes, who recently gave lectures on this subject in South Africa.[3] Vaccination to control influenza would mean the injection of millions of people every other year. Its practicability for ordinary influenza is questionable. The main justification for developing vaccines, the author points out, would be for the control of a lethal pandemic like that of 1918-19. It is possible to make potent influenza vaccines but they cause unpleasant reactions, and the results of vaccine trials have been difficult to assess. The main reason for this has been the difficulty with which the disease is diagnosed clinically. Even serological diagnosis has its pitfalls, and it has less than its normal value if the community has been vaccinated. It will be difficult to get an answer to this problem, for if viruses are constantly changing (being antigenically unstable) vaccines must be changed, and differences may occur in their potency as immunizing agents. Long-lasting immunity will be difficult to achieve. Andrewes suggests that it may be best to reserve the most effective vaccine for important people in key positions and for others who may demand it. It takes quite a long time to make vaccines of potency and safety on a large scale, which is another practical difficulty that has to be faced in any attempted control of an epidemic or pandemic.

nisasie berus. Bradley gee 'n oorsig oor die huidige posisie i.v.m. poliomiëlitisvoorbehoeding. Hy meen dat die oplossing by kunsmatige immunisasie gevind moet word maar dat dit tyd sal neem om vas te stel of blywende immuniteit verkry kan word sonder om inspuitings te dikwels te herhaal. Daar bestaan geen twyfel oor een voorbehoedingsmaatreël nie—as daar poliomiëlitis heers, moet mangeloperasies nie uitgevoer word nie.

In sy toespraak oor die gewone verkoue as 'n virusprobleem, beklemtoon Roden die moeilikhede wat met die diagnose ondervind word. Studies oor die oordra van verkoues deur die mens vorder maar stadig, maar as gevolg van dié studies is sekere hoedanighede van die virus van die gewone verkoue nou vasgestel. Daar bestaan nog geen laboratoriumtoetse nie wat die teenwoordigheid van faktore, wat verkoues veroorsaak, kan bespeur nie.

Die belangrikheid van Coxsackie-virusse en virussiektes in die trope word deur Beeman en deur Dick behandel en in 'n slotverhandeling bespreek Watson die virussiektes vanuit die gesigspunt van algemene praktyk in Engeland. Hierdie artikels sal veral vir die algemene geneesheer boei; hul gaan oor diagnose, verpleging, behandeling, epidemiologie en navorsing. Interessant is die verwysing na die afdeling van die *College of General Practitioners* wat belas is met die waarneming van epidemies. Die afdeling is ingestel om sekere aspekte van virussiektes te bestudeer soos dit deur die praktisyns waargeneem en aangeteken is.

Die oorspronklike artikels bevat inligting oor baie ander virussiekte-probleme. Watson noem die volgende as voorbeelde van vraagstukke wat op toeligting wag:—die tydsduur van aansteeklikheid voordat en nadat simptome voorkom; of die eerste geval van masels en waterpokkies in 'n huis ligter is as gevalle wat daarop volg; die epidemiologie van griep en poliomiëlitis in die tussentydperke van epidemies; ondersoekmetodes i.v.m. die epidemiologie van klierkoors en sekere ander siektes; die behandeling van akute gevalle van virussiektes en die komplikasies wat daarop volg. Miskien sal daar nie genoeg gevalle in een praktyk voorkom nie om antwoorde op die vraagstukke te voorsien nie, maar dié saamgevatte inligting en die pligsgetroue waarneming van baie geneeshere kan uiteindelik tot belangrike ontdekkings lei.

1. Simposium oor virussiekte (1954): Practitioner, **173,** 525—586.
2. Van die Redaksie (1955): S.-Afr. T. Geneesk., **29,** 29.
3. Andrewes, C. H. (1955): *Ibid.*, **29,** 2.

There has been much publicity given lately to immunization against poliomyelitis, which appears to be the main hope in preventing this dreaded disease. Bradley reviews the present position regarding poliomyelitis prophylaxis. He considers that artificial immunization offers the best hope of preventing the disease but time is required to determine whether permanent immunity will be obtained without too frequent booster injections. About one prophylactic measure there is no doubt, namely the discontinuance of tonsillectomy when poliomyelitis is prevalent.

In his discourse on the common cold as a virus problem Roden emphasizes the difficulties of diagnosis. Progress with studies of human transmission has been slow, but certain properties of the virus of the common cold have been established from them. No laboratory test has been discovered to detect the presence of the causal agents of the common cold.

The importance of Coxsackie viruses and virus disease in the tropics is considered in articles by Beeman and by Dick, and in a final paper Watson considers virus disease gauged from a country practice in England. This section will particularly interest the general practitioner; diagnosis, nursing instructions, treatment, epidemiology and research come into the picture here. Interesting is the reference to an epidemic observation unit of the College of General Practitioners which has been instituted to study certain aspects of virus disease as seen and recorded by practitioners.

For the many other problems of virus disease dealt with the original articles should be consulted. The following features are mentioned by Watson as examples of problems requiring elucidation: the duration of infectiousness before and after the onset of symptoms; whether secondary cases of measles and chicken-pox in a house are more severe than the primary case; the epidemiology of influenza and poliomyelitis between epidemics; methods for studying the epidemiology of glandular fever and certain other diseases; the treatment of acute virus diseases and their complications. In any one practice there may not be enough examples to furnish answers to such questions, but pooled information and faithful observations from many doctors may ultimately lead to important discoveries.

1. Symposium on Virus Disease (1954): Practitioner, **173,** 525-586.
2. Editorial (1955): S. Afr. Med. J., **29,** 29.
3. Andrewes, C. H. (1955): *Ibid.*, **29,** 2.

THE MEDICAL CONGRESS AT PRETORIA

We publish in this number (page XVIII) the preliminary circular issued by the Organizing Committee of the 40th South African Medical Congress, which is to be held in Pretoria in October of this year. This is Pretoria's centenary year, and a feature of this Congress is that the official opening of the 3 week's Centenary Celebrations will take place during Congress week. These celebrations should add considerably to the social interest of the Medical Congress. Moreover the jacaranda trees flower in October, and if Nature is in complacent mood the scene in which the combined celebrations will be set should be beautified with this yearly display.

The coincidence with the Centenary Celebrations renders it all the more advisable to make early reservation of hotel accommodation, and this should serve as a reminder to members to send early notice to the Honorary Secretaries of Congress of their intention to attend.

The Plenary Sessions will be devoted to the subject of *Cancer*, the many aspects of which will furnish a vast field from which to draw, and 19 Congress Sections are

announced. The Organizing Committee request contributors of papers to submit their synopses by 31 July at the latest, and the full papers by 7 September. Members, therefore, who intend to submit contributions should not delay their preparation. The policy of holding combined meetings of Sections for the discussion of subjects of common interest, which in recent years has become a feature of Congress, will be continued, and heads of Sections are asked to establish liaison with each other in order to make the necessary arrangements.

The Congress is being organized under the chairmanship of Dr. J. H. Struthers, President-Elect of the Association and Vice-Chairman of Federal Council, who is supported by a powerful team of officers and committee members and a meeting well maintaining the high standard that the South African Medical Congress has attained in recent years may be confidently anticipated. We hope it will receive the support of a large attendance of Association members.

THE DIAGNOSTIC VALUE OF URINARY GONADOTROPIC HORMONE ('FSH') ASSAYS *

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Gonadotropins or gonadotrophins are hormones producing specific stimulating effects on the gonads of both sexes. As far as is known at the present time, the *normal* production of gonadotropins is limited in man to two sites, viz. (*a*) the anterior pituitary gland and (*b*) the placenta. Gonadotropins are also produced by tumours of the placenta, ovary, testis and other organs, e.g. chorionepithelioma, hydatidiform mole, seminoma and teratoma. It is of interest that the production of gonadotropins by tumours of the pituitary gland has not been described.

The gonadotropins of the anterior pituitary gland consist essentially of 3 components, all of which are glycoproteins,[1] viz. (*a*) follicle-stimulating hormone (FSH) or gametokinetic hormone (GH), (*b*) luteinizing hormone (LH), which is similar to or identical with the interstitial cell-stimulating hormone (ICSH), and (*c*) luteotropic hormone (LTH), which is probably identical with the lactogenic hormone.

The scope of this paper is limited to a discussion of the clinical usefulness and application of the assay, in the urine of 50 males and non-pregnant females, of a gonadotropin presumably elaborated in the anterior pituitary gland. It is referred to as follicle-stimulating-hormone, or FSH, since the assumption is made in the assay method used in these experiments that FSH stimulates the production of oestrogens in the immature female mouse. The resultant increase in weight or size of the uterus is then used as the indicator of the FSH content of the extracts. This assumption rests on experimental work involving the use of impure gonadotropic extracts, and the demonstration that, as the Graafian follicles increase in size, the liquor folliculi which is formed contains oestrogens. However, using 'pure' FSH, Greep, van Dyke and Chow [2] reported in the hypophysectomized rat that the Graafian follicles increased in size, but did not secrete oestrogen as measured by the response of the uterus and vagina. The addition, however, of small quantities of luteinizing hormone (LH) immediately resulted in oestrin production.

Since the biological effect of FSH by definition is the stimulation of growth of Graafian follicles it would appear preferable to determine the extent of follicular growth and development as the index of FSH activity. However, here too difficulties arise. For example, contamination with other gonadotropins will augment the ovarian response to FSH,[3] and in the hypophysectomized rat the augmentation occurring at low doses shows first in enlargement of follicular size. Secondly, the crude nature of urinary extracts also introduces complications since they almost certainly contain a mixture of gonadotropins.

It is evident, therefore, that an assay procedure simple enough for clinical use would probably not be specific for follicle-stimulating hormone (FSH). The term 'urinary FSH assays' has, however, gained so wide an acceptance that it is convenient to retain this term for the present. The biological methods in present use are only roughly quantitative, owing to the inherent variability of animal response, particularly with urines of low FSH content, and the unknown degree of synergism between the gonadotropins extracted from the urine and the minute amounts present in the pituitary of the assay animal, even though this is immature. Howard *et al.*,[4] for example, feel that the minute amounts of LH necessary for the ovarian follicles to produce oestrogen may be already present in the pituitary of the infantile mouse used in the FSH assay. They do not, however, deny that LH is also present in at least small amounts in some, if not in all, of the urine extracts used.

EXPERIMENTAL

No claim is made for originality in the method described below but the procedure is described in some detail for the convenience of other clinical laboratories who may wish to use this technique. The extraction of the urine is based on Dekanski's modification of Scott's method,[5, 6] and in some of its details it follows the method in use at St. Thomas' Hospital, London. The method of bio-assay is essentially that carried out by Albright and his colleagues [7] at Boston, using the mouse uterine technique.

Principle. The gonadotropins are adsorbed on to kaolin at an

* A summary of this paper was presented at a meeting of the Transvaal Society of Pathologists held in Johannesburg on 11 March 1954.

acid pH, leaving some water-soluble toxic substances in the supernatant, which is discarded. The gonadotropins are then eluted from the kaolin by alkali. After neutralization the eluate is treated with cold acetone, which precipitates the protein gonadotropins, leaving steroids such as the sex hormones in the supernatant fluid, which is again discarded. The precipitate is dried, washed with ether, and dried until free of all traces of acetone. The dry brownish powder is dissolved in distilled water and suitable aliquots injected into mice. This method produces a relatively non-toxic extract and rarely causes death of the mice.

Details of Method. Collect a 24-hour specimen of urine without preservative. Measure the volume, and if less than 2 litres make up to 2 litres with water.

Extraction. Acidify with 20% HCl (1 part concentrated hydrochloric acid and 4 parts distilled water) to pH 4·0, using a pH paper of suitable range. Add 100 ml. of 20% aqueous kaolin (acid-washed) suspension per litre (of original volume) of urine. Allow to stand at room temperature for 1-2 hours, shaking at intervals. Leave overnight at approximately 4°C. Remove the greater part of the supernatant fluid with the suction pump and transfer the remainder with the kaolin sediment to 250 ml. centrifuge cups. Centrifuge for 15-20 minutes at approximately 2,000 r.p.m. and discard the supernatant fluid. Add to the kaolin deposit 50 ml. of N/10 NaOH per litre (of original volume) of urine. Grind up the sediment thoroughly in the NaOH solution with a glass rod, making sure that all lumps are completely broken up. Centrifuge again for 15-20 minutes at ± 2,000 r.p.m. Transfer supernatant to suitable container, e.g. a vaco-litre bottle, and adjust pH to 5.0 with 20% HCl. Measure the final volume and precipitate with 5 volumes of cold acetone. A flocculent precipitate should form almost immediately. Allow to stand for 4 hours, shaking at intervals. Remove part of the supernatant if possible as above and spin the remainder in a 250 ml. centrifuge cup for 10 minutes at 2,000 r.p.m. Decant supernatant carefully and discard. The precipitate is dried by blowing air gently over it for 30-60 minutes, or even longer, *until almost dry*. Approximately 10 ml. ether is then added to the precipitate and stirred for a few minutes, the ether decanted, and the drying process repeated. The ether wash is repeated if necessary *until all the acetone has been removed* and a dry powder remains. This powder is usually amorphous and brown-coloured.

As a routine, 8 immature female mice, approximately 20 days old and 6-8 g. in weight, are used for each assay. Two mice are used at assay levels of 6, 12, 24 and 48 units.

Bio-assay

Nine ml. of distilled water is added to the dried powder in the centrifuge bottle, stirred well with a glass rod, and allowed to stand overnight at approximately 4°C. Centrifuge, and decant the supernatant into a clean test-tube.

0·25 ml. of this supernatant is injected subcutaneously into the lower part of the back twice daily for 3 days into each of 2 mice. Each mouse thus receives 1·5 ml. of the total 9 ml. i.e. ⅙ of the total extract. A positive response shown by the mice at this level means that 1 mouse unit is present in ⅙ of the extract, and therefore 6 *mouse units in the total 24-hour specimen.*

Serial dilutions are prepared from 4 ml. of the above supernatant to give 1 : 1, 1 : 2 and 1 : 4 concentrations of the original extract. Positive results with these dilutions used in the above manner would then correspond respectively to 12, 24 *and* 48 *mouse units in the total 24-hour specimen.*

All the solutions are kept in the refrigerator at ± 4°C between injections. In case further dilutions may be required, 4 ml. of the last dilution are placed in the deep freeze or in the freezing unit of a refrigerator. If a positive result is found at the 48-unit level, this solution is diluted further to be tested at 96, 192, 384 and 768 unit levels. Where less than 6 units of urinary gonadotropins are found, a second 24-hour specimen may be extracted and tested at the 3-mouse-unit level by dissolving it in 4·5 ml. saline. This barely gives 3 ml. of supernatant and is usually just sufficient for injecting 2 mice.

The mice are killed by coal gas on the 4th day, and the uteri inspected. If required, the uteri are carefully dissected out, freed of connective tissue, gently pressed between filter papers to remove free fluid and then weighed. The uterine weight of a 7-g. mouse has usually been found to be just less than 6 mg. and always less than 7 mg.

We have not used the original Mouse Uterine Unit of Levin and Tyndale [6] but, following Klinefelter *et al.*,[7] *one Mouse Uterine Unit* is here taken to be present in the highest dilution of extract which, when injected twice daily for 3 days, produces, 72 hours after the first injection, an obvious enlargement of the uterus of the test animal. The uteri are weighed only when there is questionable enlargement. If the uterus weighs more than 7 mg. after the fluid has been expressed by pressure between layers of filter paper, it is considered to be enlarged.

We report 'FSH' in inverted commas, because it does not appear justifiable to assume at the present time that pure FSH, which stimulates follicle growth, is also responsible for the oestrogen production necessary to stimulate uterine growth.

The normal ranges reported for the various bio-assay methods used vary considerably. Evans and Simpson's review [3] should be consulted by those particularly interested in this aspect of the subject. Although we have not as yet examined an extensive series of normal subjects, the normal range for the method as described above in adult males and females appears to be 6-24 units. In children until the onset of puberty, gonadotropins are below 6 M.U. In view of the ranges quoted in the literature, it may be preferable at the present time to extend the extreme upper range for normal adults to 48 units.

RESULTS AND DISCUSSION

The results in 50 patients in whom 'FSH' assays were undertaken are shown in the following tables. The cases are classified according to the presenting clinical problem or most obvious endocrinopathic state. This method of presentation was selected so as to illustrate the circumstances in which 'FSH' assays may have considerable differential diagnostic value:

(1) Suspected hypopituitarism (Table I).
(2) Delayed adolescence (Table II).
(3) Amenorrhoea (Table III).
(4) Hypogonadism in males (Table IV).
(5) Sexual precocity (Table V).
(6) Hirsutism and/or virilism (Table VI).
(7) Sterility (Table VII).

(1) *Hypopituitarism* (Table I)

It has already been stated that no tumour of the anterior pituitary gland is known to produce excessive quantities of gonadotropin, nor has hyperpituitarism with hypersecretion of gonadotropins been described. In clinical states, however, in which *hypopituitarism* is suspected, FSH assays are of great importance, since it

TABLE I. SIX CASES OF SUSPECTED HYPOPITUITARISM

Case	*Initials*	*Age*	*Sex*	*Diagnosis*	*Urinary FSH (Mouse Uterine Units per 24 hours)**	
1	E.S.	40	F	Pituitary myxoedema		− 6
2	J.O.	23	F	Sheehan's syndrome		− 3
3	P.	45	F	Calcified tumour of pituitary		− 6
4	A.A.	21	F	Early anorexia nervosa	+24	−48
5	H.P.	20	F	Anorexia nervosa with secondary hypopituitarism		− 6
6	I.J.	8	F	Dwarfism (? primordial, ? pituitary)		− 6

* In reporting results of FSH assays the highest level showing a positive response is preceded by a plus sign and the lowest level giving a negative response is preceded by a minus sign. If results were negative at all levels, the figure shown is the lowest at which bio-assay was performed.

is the most common of the 'tropic' hormones to fail. Such deficiency may be 'selective' or may be accompanied by evidence of deficient thyrotropic hormone (as in case 1) and deficient adrenocorticotropic hormone (ACTH) production, i.e. panhypopituitarism—e.g. Sheehan's syndrome (case 2) and Simmonds' disease.

In case 1, myxoedematous since childhood, the possibility of the myxoedema being pituitary in origin was considered on clinical and biochemical grounds. Evidence in favour of the hypothyroidism being due to hypopituitarism was an FSH excretion below the normal level since this is usually normal in hypothyroidism.[9] Case 2 was a typical example of Sheehan's syndrome [10]—post-partum necrosis of the pituitary gland. In this patient, where destruction of the anterior pituitary gland appeared fairly certain from the clinical features and history, FSH excretion could not be demonstrated even at the 3-unit level. With an organic lesion involving the pituitary gland, however, FSH excretion is again low. In case 3, where a calcified tumour of the pituitary was found at operation, no FSH could be demonstrated in the urine.

FSH assays are also of crucial importance in the differentiation of cases of anorexia nervosa (cases 4 and 5) from organic lesions producing hypopituitarism. In early cases FSH may be within normal limits (case 4), whereas in more advanced cases (case 5), evidence of secondary hypopituitarism is present, and the prognosis is correspondingly more serious. Since the approach to therapy in anorexia nervosa and hypopituitarism is fundamentally different, the importance of differentiating these two states is obvious.

Wilkins,[11] in his classification of the various causes of dwarfism, lists the types of dwarfism due to endocrine disturbances and genetic causes, and goes on to say that 'the distinction between patients with stunted growth and delayed adolescence, and those with pituitary deficiency or with genetic dwarfism is often exceedingly difficult to make during childhood'. No attempt can be made here to discuss the investigation of a case of dwarfism as such but, where it is impossible to determine the cause of the stunted growth, the observation of the pattern of sexual development in early adolescence will throw light on whether there is a genetic defect, pituitary deficiency or delayed adolescence. In primordial or genetic dwarfism, other than in the special type associated with ovarian agenesis (Turner's syndrome), in which very high titres of FSH are found (Case 28—Table III), sexual maturation is normal and FSH levels are normal. The pituitary dwarf on the other hand remains sexually infantile, and FSH is not demonstrable in the urine. In Case 6, the absence of FSH in the urine is to be expected in view of the age of the patient. Assay of FSH towards the time of puberty may, however, distinguish between primordial or genetic dwarfism and hypopituitarism in this case.

(2) *Delayed Adolescence and Sexual Infantilism* (Table II)

Although, by the method of bio-assay described here, FSH excretion cannot be demonstrated until puberty, there are nevertheless 3 clinical problems in childhood where information regarding the secretion of gonadotropins by the anterior pituitary gland may be sought. The 1st, which is the differential diagnosis of dwarfism in childhood, has already been discussed. The 2nd is the investigation of sexual infantilism persisting into adolescence (Table II). The 3rd problem is the differentiation of cases of sexual precocity (Table V). The first 2 problems may, and commonly do, overlap.

Sexual infantilism persisting into adolescence poses in the first place the problem of determining whether this is due to delayed puberty, in which case normal sexual maturation will eventually occur even as late as 17-18 years of age, or whether there is an organic disorder in the hypothalamus, the pituitary gland or the gonads. Wilkins [12] clearly indicates the value of FSH assays in these cases.

In the early 'teens the demonstration of an FSH excretion of 6-12 units would lead one to expect normal sexual maturation, and therefore to advise that treatment with gonadotropin preparations or sex hormones should be withheld. An absence of FSH excretion should be interpreted with caution until 16-17 years of age, after which time it can be considered to indicate sexual infantilism due to pituitary or hypothalamic disorders.

In cases 7, 8, 9 and 10 the presenting problem was to differentiate a delayed onset of adolescence from a more severe organic endocrinological disorder. Case 7 was tall and thin, with eunuchoid proportions and no secondary sex development. Case 8 was obese but again showed no secondary sex development. In neither case could urinary FSH be demonstrated. Case 9 also showed a delayed onset of puberty with an absence of demonstrable FSH in the urine but, since this patient was of short stature, the question arose as to whether there was also a lack of pituitary growth factor. In none of these cases could the available evidence exclude a 'delayed' adolescence. These cases were therefore advised to return for reassessment and a further FSH assay after one year. During this period hormonal therapy should be

TABLE II. EIGHT CASES IN WHICH THE DIFFERENTIAL DIAGNOSIS LAY BETWEEN DELAYED ADOLESCENCE AND SEXUAL INFANTILISM

Case	*Initials*	*Age*	*Sex*	*Diagnosis*	*Urinary FSH (Mouse Uterine Units per 24 hours)*
7	A.G.	14	M	? Delayed adolescence	− 6
8	I.A.	13	M	? Delayed adolescence	− 6
9	B.H.	14	F	Delayed adolescence +dwarfism (? hypopituitarism)	− 6
10	S.T.	16	F	? delayed adolescence	− 6
11	M.F.	16	M	Sexual infantilism, ? hypopituitarism	− 6
12	H.S.	16	M	Sexual infantilism, ? hypopituitarism (cyst of pituitary excised in childhood)	± 6 −12
13	S.	13	M	Obesity with ? small genitalia, ?? Froehlich's syndrome	± 6 −12
14	F.C.	12	M	Sexual infantilism due to primary testicular deficiency	+12 −24

withheld. Testicular biopsy, or a study of vaginal cytology, may also be necessary before a final diagnosis can be made.

Case 10 offered an interesting variant of this problem. This patient was a girl aged 16 years with primary amenorrhoea. Breast development and pubic hair growth, however, appeared to be normal. Primary ovarian failure (see section 3) was considered unlikely in view of the lack of demonstrable FSH in the urine. The presence of mammary growth suggested that some oestrogen was being produced by the ovaries, which were as yet perhaps being inadequately stimulated by gonadotropins, and a study of the vaginal cytology for evidence of oestrogen stimulation was therefore suggested but the patient's co-operation could not be obtained. Here again it would appear preferable to keep this type of case under observation for some while before having recourse to oestrogen therapy, which could conceivably still further depress endogenous ovarian function.

The remaining cases in Table II provide features contrasting with the cases already discussed. Cases 11 and 12, both 16 years of age, provided good clinical evidence of hypopituitarism with sexual infantilism—very small testes and no secondary sex characters, dwarfism, and general immaturity of appearance. In case 12 a cyst of the pituitary had been removed several years previously, and testicular biopsy now showed complete absence of spermatic tubules and interstitial cells. Since there was obviously no reasonable expectation of such testes ever producing androgens or spermatozoa, replacement therapy with testosterone was commenced, with excellent results, not only in the development of secondary sex characters but also in general well-being, initiative, and drive. Case 13, which should be contrasted with Cases 7 and 8, was an obese boy of 13 years whose genitalia were buried in the excess of fat around the pubis, and appeared small for his age. He serves as an example of a common clinical problem, viz. the fat boy who at puberty does not appear to be maturing normally and in whom the possibility of Froehlich's syndrome is inevitably raised. It should be remembered that Froehlich's syndrome is rare, and that fat boys usually mature normally, although puberty may be delayed. The differential diagnosis was made by FSH assay and, since this was normal, Froehlich's syndrome was excluded. Case 14 is included as providing a very interesting early example of the Klinefelter-Heller syndrome.[13, 14] Clinically this case appeared to be very similar to Case 13—a boy aged 12 years, stunted in growth, with small testes and no secondary sex characters. The *high FSH excretion for age*, however, excludes hypopituitarism and also excludes delayed adolescence. With this amount of FSH the testes should have shown normal pubertal development. The small testes were therefore taken to indicate a primary testicular deficiency or failure. In this case a testicular biopsy was unfortunately refused, but the diagnosis was confirmed by a further FSH assay 1 year later (when aged 13 years) which showed an increase in the excretion to 48 units. In this patient, therefore, replacement therapy with testosterone was advised, as endogenous production of testosterone could not be expected.

(3) *Amenorrhoea* (Table III)

We turn now to a discussion of 17 cases of amenorrhoea in which FSH studies were carried out. The differential diagnosis of amenorrhoea (or oligomenorrhoea) will not be considered here; but from the endocrinologist's point of view it is of interest and sometimes of importance to determine the level of the functional or organic disturbance in the endocrine system which leads to amenorrhoea. As far as is known today, it is probable that depressed ovarian function must be present in all cases (other than pregnancy or pathological over-production of oestrogens leading to endometrial hyperplasia and temporary suppression of menses). With a primary ovarian deficiency the pituitary-ovarian balance is disturbed, leading in many cases to excessive production of FSH. Where the ovaries fail to develop, e.g. in Turner's syndrome,[15] the level of FSH excretion may rise considerably (case 15). After oestrogen therapy this level drops rapidly (case 16). A follow-up of both these cases after a few months on oestrogen therapy showed a decrease in FSH to 6-12 units. Similarly an increase of FSH excretion occurs at or after the menopause, this again suggesting a primary ovarian failure (cases 17 and 18). In cases of premature onset of the menopause (cases 19 and 20) the FSH excretion rises to the upper limits of normal or beyond.

Cases of primary ovarian deficiency may occur without the other stigmata of Turner's syndrome, and such patients may present with the clinical features associated with eunuchoidism. The differentiation from eunuchoid-

TABLE III. SEVENTEEN CASES OF AMENORRHOEA IN WHICH THE DIFFERENTIAL DIAGNOSIS LAY BETWEEN A GONADOTROPIN DEFICIENCY, AN OVARIAN DEFICIENCY AND A NON-ENDOCRINOPATHIC ETIOLOGY

Case	*Initials*	*Age*	*Sex*	*Diagnosis*	*Urinary FSH (Mouse Uterine Units per 24 hours)*
15	M.V.	19	F	Ovarian agenesis (Turner's syndrome)	+192–384
16	C.M.	30	F	Ovarian agenesis (Turner's syndrome) (Previous therapy with oestrogens)	+48 –96
17	J.B.	59	F	Post-menopausal (normal control)	+96 –192
18	E.B.	65	F	Post-menopausal (normal control)	+24 –48
19	T.L.	36	F	Premature menopause	+48 –96
20	J.N.	29	F	Premature menopause	+48 –96
21	R.	35	F	Eunuchoidism due to primary ovarian deficiency	+192 –384
22	S.G.	32	F	Eunuchoidism due to specific gonadotropin deficiency	–12
23	D.E.	39	F	Chronic anxiety state	+ 6 –12
24	J.C.	30	F	Anxiety state	– 6
25	J.C.	26	F	Obesity of hypothalamic origin	–12
26	A.D.	18	F	Thyrotoxicosis	– 6
27	S.S.	39	F	Thyrotoxicosis	+24 –48
28	C.G.	30	F	? Cushing's syndrome	+24 –48
29	N.	±50	F	? Cushing's syndrome	– 6
30	M.M.	38	F	Obesity (? Cushing's syndrome)	+12 –24
31	W.B.	17	F	Obesity	+ 6 –12

ism due to hypopituitarism can then be made on the basis of a high FSH excretion. Two cases of this type are included in this series. Case 21 is an example of eunuchoidism due to primary ovarian deficiency (in view of the high FSH excretion), whereas case 22 may be an example of a primary gonadotropin deficiency,[16] since no FSH excretion could be shown at the lowest level of FSH which could be tested (more concentrated extracts being toxic to the test animals).

Klinefelter *et al.*[7] drew attention to these differences very clearly in 1943, and concluded their paper with the statement 'It would appear that with the tests for excretion levels of follicle-stimulating hormone, one can divide cases of hypo-estrinism into 3 categories: (*a*) ovarian hypoestrinism due to primary ovarian insufficiency and associated with increased excretion of follicle-stimulating hormone, (*b*) pituitary hypoestrinism due to primary lack of production of follicle-stimulating hormone and associated with decreased excretion of it, and (*c*) hypothalamic hypoestrinism due to disturbance in the hypothalamic-pituitary nervous pathway and associated with a normal excretion level of follicle-stimulating hormone. These authors suggest that lack of production of oestrogen with a normal excretion of FSH might be due to lack of production of LH by the anterior pituitary gland. They argue that by analogy with the conditions obtaining in other mammals such lack may be due to the failure of the hypothalamic-pituitary nervous pathways to release LH from the anterior pituitary. The complexity of the hypothalamic-pituitary pathways is still far from being clearly understood, but an awareness of such a third group is useful for the inclusion of cases of amenorrhoea or oligomenorrhoea which appear to be 'psychogenic' in type. Case 23 and cases 43-45 (Table VII) possibly fall into this group. In case 24 (psychogenic amenorrhoea) the pituitary depression has led apparently to a decrease in FSH as well as LH production. In case 25, where a diagnosis of hypothalamic obesity with amenorrhoea was made, FSH excretion was again low.

In other endocrine disorders and in simple obesity (cases 26-31) the results of the FSH assays are of no assistance in diagnosis. Escamilla[9] also reported normal FSH values in such conditions as thyrotoxicosis and Cushing's syndrome, but no mention is made whether amenorrhoea was present. In such cases the pathogenesis of the amenorrhoea has not, to our knowledge, been clearly established.

(4) *Hypogonadism in Males* (Table IV)

Klinefelter *et al.*[13] in 1942 described a hypogonadal syndrome with gynaecomastia, and an increased excretion of FSH. Heller and Nelson[14] in 1945 extended this work to include cases of hypogonadism without gynaecomastia.

These pioneering studies have been followed by many others which have considerably clarified the relationships between hypogonadism, bodily habitus, hormonal assays and testicular biopsy examinations. Sohval[17] offers a working classification in which cases of hypogonadism are grouped according to whether they originate in the testes or elsewhere, and whether they begin before or after the completion of puberty. In primary testicular failure FSH excretion is increased, whereas in hypogonadism due to extragenital causes FSH is low or absent. The level of FSH excretion therefore helps in determining the etiology of the hypogonadism and is a valuable pointer to treatment. Where the deficiency is shown to be primarily testicular (high FSH excretion) as in cases 32 and 33, substitution therapy with testosterone is indicated. Stimulation therapy with gonadotropins should however be tried where a low or absent FSH excretion suggests that testicular deficiency may be secondary to a lack of normally-produced gonadotropins.

TABLE IV. TWO CASES OF HYPOGONADISM IN MALES IN WHICH THE DIFFERENTIAL DIAGNOSIS LAY BETWEEN A PRIMARY GONADOTROPIN DEFICIENCY AND A PRIMARY TESTICULAR DEFICIENCY

Case	*Initials*	*Age*	*Sex*	*Diagnosis*	*Urinary FSH (Mouse Uterine Units per 24 hours)*	
32	B.L.	25	M	Eunuchoidism due to primary testicular deficiency (Klinefelter-Heller syndrome)	+192	−384
33	F.K.	36	M	Primary testicular deficiency (Klinefelter-Heller syndrome)	+384	−768

(5) *Sexual Precocity* (Table V)

The value of FSH assays in the study of cases of sexual precocity is considered with reference to 4 cases. True or constitutional (usually idiopathic) precocity apparently results from pituitary gonadotropic stimulation of the gonads, but no tumour or other lesion in the pituitary gland has ever been found. In a small minority of cases, however, organic lesions in the region of the pineal gland and hypothalamus have been demonstrated. Since true precocity is due to secretion of pituitary gonadotropins, the presence of FSH in the urine establishes the diagnosis (case 34). In normal

TABLE V. FOUR CASES OF SEXUAL PRECOCITY

Case	*Initials*	*Age*	*Sex*	*Diagnosis*	*Urinary FSH (Mouse Uterine Units per 24 hours)*	
34	K.T.	4	M	Isosexual precocity (constitutional or idiopathic)	+24	−48
35	E.R.	6	M	Isosexual precocity (suprarenal hyperplasia)		− 6
36	H.R.	9	F	Heterosexual precocity due to adrenogenital virilism (suprarenal hyperplasia)		− 6
37	E.G.	8	F	Isosexual precocity (pituitary tumour removed 4 years previous to test), hypothalamic obesity, diabetes insipidus		− 6

childhood FSH is not demonstrable in the urine. The diagnosis in case 34, a child aged 4 years, was confirmed by testicular biopsy, which showed active spermatogenesis and the picture of an early pubertal testis. In case 35, a boy aged 6 years (to be contrasted with case 34), the patient also showed isosexual precocity, but that this was a pseudo-precocious puberty was established by the absence of demonstrable FSH in the urine (less than 6 units), and confirmed by testicular biopsy, which showed a pre-pubertal testis approximately normal for the age of the patient, and by a high neutral 17-ketosteroid excretion for age (10-11 mg.) The latter finding almost certainly indicates a suprarenal hyperplasia or tumour, provided that an intestitial-cell tumour of the testis can be excluded. Case 36, a sister of case 35, also showed precocious sexual development, apparently from birth, but the chief manifestations were heterosexual in type. The final diagnosis in this case was suprarenal hyperplasia (neutral 17-ketosteroid excretion 17-18 mg. per 24 hours). Here again, since the origin of the 'sex hormones' was the suprarenal gland and not the gonad, absence of FSH in the urine could be anticipated. Case 37 is of considerable interest—isosexual precocity in a little girl aged 8 years, who 4 years previously had a pituitary tumour removed. Since the patient showed marked obesity, polyphagia, and diabetes insipidus, it appeared probable that a lesion (? traumatic) of the hypothalamus was responsible for the precocity. However, in this case the absence of urinary FSH led to an alternative possibility being considered, viz. the presence of gonadotropins in the whole-pituitary powder (administered by nasal insufflation) which was used to control the diabetes insipidus, since the daily dose of this powder was found to contain approximately 48 mouse units.

(6) *Hirsutism and/or Virilism* (Table VI)

Case 38, a case of female pseudohermaphroditism due to suprarenal hyperactivity (no tumour was demonstrable at operation) is included to show again that increased FSH excretion does not accompany suprarenal virilizing lesions and that the androgenic hormones produced in the suprarenal gland may in fact suppress gonadotropin production by the pituitary gland. Escamilla,[9] however, reported the presence of FSH in many of his cases with an actual slight increase in about half. Cases 39 and 40 were diagnosed clinically as cases of the hyperthecosis syndrome (Culiner and Shippel [18]) or Stein-Leventhal syndrome.[19] This was proved by ovarian biopsies, and both showed levels of FSH excretion at the upper limits of reported normals, and somewhat greater than the normal values usually found by us. The significance of this is not clear, but the increased FSH production may be associated with the enlarged cystic follicles sometimes found in the ovaries of these cases, rather than with the marked hyperplasia of theca-cell elements which is a feature of this syndrome (Shippel [20]). Escamilla,[9] however, reported normal FSH in 3 cases and an elevated FSH excretion in one patient. In a third case of marked hirsutism (case 41) a high normal FSH excretion was found. This patient had undergone unilateral adrenalectomy with only temporary relief. The recurrence of hirsutism and the level of FSH excretion may however indicate that the ovary and not the suprarenal gland is abnormal.

TABLE VI. FOUR CASES OF HIRSUTISM AND/OR VIRILISM

Case	*Initials*	*Age*	*Sex*	*Diagnosis*	*Urinary FSH (Mouse Uterine Units per 24 hours)*	
38	W.	20	F	Adrenogenital virilism due to suprarenal hyperplasia		− 6
39	E.R.	33	F	Hyperthecosis syndrome	+48	−96
40	E.P.	31	F	Hyperthecosis syndrome	+48	−96
41	F.G.	25	F	Hirsutism (? adrenogenital syndrome. ? hyperthecosis syndrome)	+24	−48

(7) *Sterility* (Table VII)

Four cases of female sterility (cases 42-45) and 5 cases of male sterility (cases 46-50) are recorded, where the FSH excretion was determined as part of a study to discover any accompanying endocrinological abnormality. The 4 female cases showed no obvious endocrinopathy and the FSH excretion was normal. The possibility has not however been excluded that, despite the

TABLE VII. NINE CASES OF STERILITY WHERE GONADOTROPIN ASSAYS WERE DONE AS PART OF THE STUDY TO DETERMINE THE UNDERLYING ETIOLOGY

Case	*Initials*	*Age*	*Sex*	*Diagnosis*	*Urinary FSH (Mouse Uterine Units per 24 hours)*	
42	Z.M.	33	F	Sterility. No obvious endrocrinopathy and menstrual history normal	+12	−24
43	B.D.	22	F	Sterility. No obvious endrocrinopathy but oligomenorrhoea present	+ 6	−12
44	S.R.	25	F	Ditto.	+12	−24
45	E.J.	27	F	Ditto.	+12	−24
46	J.H.	30	M	Azoospermia and eunuchoidism, small testes (? selective deficiency of Gonadotropins)	+ 6	−12
47	D.H.	24	M	Azoospermia, impotence, obesity (? small testes, selective deficiency of Gonadotropins)	± 6	−12
48	H.B.	±30	M	Oligospermia, normal-sized testes but testicular biopsy showed impaired spermatogenesis. No obvious endocrinopathy	+24	−48
49	L.J.	±30	M	Oligospermia, small testes (no biopsy permitted). No obvious endocrinopathy	+12	−24
50	C.	±25	M	Azoospermia (bilateral mumps orchitis 2 years ago), normal-sized testes	+48	−96

apparently normal production of FSH, there is insufficient LH to cause ovulation. However, from the standpoint of the present discussion it is apparent that in those cases of sterility where a normal FSH excretion is found the assay does not assist in explaining the etiology of the sterility. It does, however, suggest that no gross ovarian or pituitary abnormality is present.

In male sterility several studies attempting to correlate testicular deficiency with FSH excretion levels have been reported. Thus Howard *et al.*[4] recorded the clinical findings with testicular biopsy results and excretion levels of FSH in 141 men with testicular deficiency. They classified their cases into 3 groups—cases with low FSH, normal FSH and high FSH excretion respectively. Their classification of cases contributes in no small measure to our understanding of cases showing azoospermia. In some cases sufficient evidence can be obtained to indicate whether there is an associated endocrine disturbance or not, and whether this is a primary testicular or pituitary deficiency. Although testicular biopsy should always be advised and may provide crucial information, nevertheless permission for this procedure is often refused. Even in its absence, however, a reasonably accurate diagnosis may be provided by FSH assays. Thus a raised FSH excretion occurs after mumps orchitis, and in case 50, where azoospermia was present in an apparently normal, healthy, potent young male adult with a history of mumps orchitis 2 years before the assay, the excretion of 48 units is compatible with the diagnosis. The bodily habitus of cases 46 and 47, both of whom showed azoospermia, suggested some degree of hypopituitarism, and the low normal level of FSH excretion tends to confirm this impression. In cases 48 and 49, however, with a normal FSH excretion the etiological factors responsible for the sterility were not apparent, but neither case appears to be primarily due to endocrine defects.

SUMMARY AND CONCLUSIONS

Urinary gonadotropin ('FSH') assays are reported on 50 males and non-pregnant females, and the clinical applications of the results are discussed.

The assay method used is described in detail.

In suspected hypopituitarism, FSH assays are of importance since

(*a*) it is the most common of the 'tropic' hormones to fail, and

(*b*) it permits differentiation between anorexia nervosa and organic hypopituitarism.

In adolescence FSH assays are of value in investigating cases of dwarfism, in differentiating between delayed puberty and sexual infantilism, and in determining the type of sexual precocity.

FSH assays assist in determining the level of the functional or organic disturbance in the endocrine system which leads to amenorrhoea. In the study of hypogonadism in males, FSH assays are of fundamental importance.

Since true or constitutional precocious puberty is due to secretion of pituitary gonadotropins, the presence of FSH establishes the diagnosis, whereas the absence of FSH indicates a pseudo-precocious puberty. Similar considerations suggest that suppression of FSH may accompany suprarenal virilizing lesions.

In cases of sterility a normal FSH excretion suggests that no gross pituitary or gonadal abnormality is present. An abnormal excretion would however indicate that the sterility is only one manifestation of an endocrinopathy.

Our thanks are due to Dr. S. Sims, Dr. J. Gluckman and Dr. W. Lewin for providing many of the facilities used in this investigation; to Dr. S. Lopis, Endocrine and Metabolic Clinic, Johannesburg Hospital, for allowing us access to a number of the cases reported, and to our medical colleagues in practice for permission to report our FSH assays on their cases and for their cooperation in supplying us with the clinical notes.

It is also a pleasure to acknowledge our indebtedness to Dr. H. B. Stein, Acting Head of the Department of Clinical Pathology, for considerable help in the preparation of this paper.

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IDIOPATHIC HYPOPARATHYROIDISM

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Idiopathic hypoparathyroidism is a rare disease. Drake, Albright, Baur and Castleman [3] fully described it in 1939. Only 50 or 60 proven cases (de Mowbray,[2] 1953) have been reported in the literature. As far as we know the following is the first reported case in an African.

CASE REPORT

A 38-year old African female was admitted to Coronation Hospital, Johannesburg, on 28 October 1950, complaining of numbness and cramp-like pains in the hands and feet for the preceding 24 hours. She had also vomited several times during this period and had had hiccoughs for a few hours before admission. Apart from occasional palpitations there was no other significant history.

Physical Examination

The patient was moderately obese. She had typical carpo-pedal spasms. The Chvostek, Trousseau and Erb signs were all strongly positive. She was hypertensive, blood pressure being 180/120 mm. Hg, with a heaving cardiac impulse and a loud apical systolic murmur. The skin, hair and nails were normal. Both optic fundi were normal and no cataracts were noted. The thyroid gland was not palpable and there was no evidence of any previous operative procedure on her neck. The rest of the physical examination was negative.

Laboratory Studies

Haemoglobin 14·6 g.%. White cells 6,400 per c. mm. (differential count normal). Wassermann reaction negative. Serum alkali reserve 57 vols.%. Blood urea 28 mg.%. Liver function tests normal. Plasma proteins 6·5 mg.%. Serum calcium 4·9 mg.%. Serum phosphorus 6·8 mg.%. (Numerous investigations showed a range of serum calcium from 4 to 6 mg.% and serum phosphorus from 6 to 8 mg.%.)

Urea clearance test—89% of average normal renal function. Urinary concentration test—specific gravity up to 1022. Urine—N.A.D.; culture (numerous catheter specimens)—no growth.

Intestinal fat absorption—87% absorption of fat intake per day. Total stool solids analysis—29% fat, of which 19% was unsplit. No parasites found in the stools.

Radiology. Skull and long bones—N.A.D. Chest—markedly enlarged heart affecting chiefly the left ventricle. Intravenous pyelogram—no gross abnormality of the pelves; excretion of the dye moderately good.

Electrocardiography. PR interval 0·16. Qt interval 0·4. QTc interval 0·52. T waves isoelectric in leads V 2, 3, 4 and 5.

Treatment and Progress

Initially 10 ml. of a 10% solution of calcium gluconate was given intravenously, followed by 10 g. of calcium lactate 3 times a day by mouth and 2 pints of milk plus 120,000 units of calciferol daily. This relieved the patient's symptoms but did not appreciably alter the biochemistry. Finally the daily administration of 3 ml. of A.T. 10 (dihydrotachysterol) produced a rapid restoration of the blood calcium and phosphorus levels to normal (Fig. 1).

The patient was discharged on a daily maintenance dose of a ½ to 1 ml. of A.T. 10. Her subsequent attendance at the out-patient department was extremely irregular and she was re-admitted

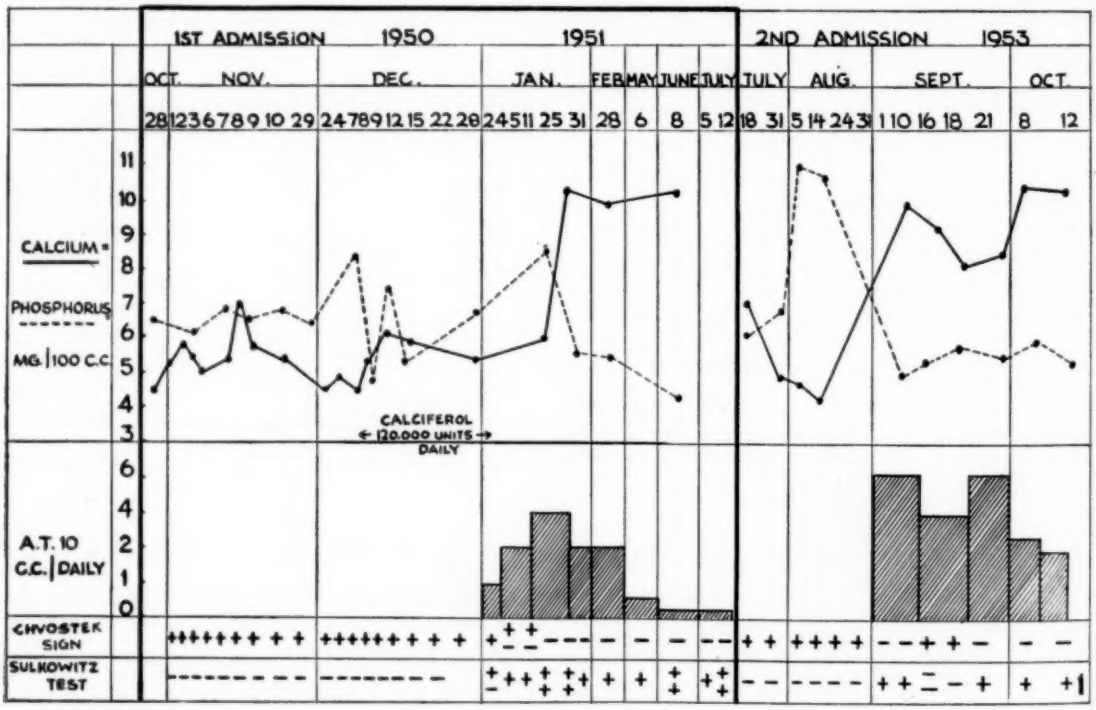

Fig. 1.

twice during the following 3 years, on the first occasion for treatment with hexamethonium compounds in an attempt to control her hypertension, which was unsuccessful.

READMISSION TO HOSPITAL

The patient was admitted to hospital for the 3rd time on 18 August, 1953 approximately 2½ years after the onset of her symptoms, on account of the return of her tetany, due mainly to neglect of therapy.

Examination revealed a similar clinical picture to that on her first admission, viz. marked carpo-pedal spasm with positive Chvovstek and Trousseau signs. Vomiting and hiccough were again prominent. In addition she had early signs of congestive cardiac failure—engorged neck veins, moderate hepatomegaly and mininal peripheral oedema.

Further, the skin was now dry and had a peculiar texture which could best be likened to that of blotting paper. Distributed over the 'butterfly area' of the face were sharply demarcated, irregular patchy, brown pigmented areas. Bald patches were apparent on her head affecting chiefly the frontal and occipital regions. The hair was brittle and fell out easily. Her eyebrows and eyelashes had become thin and there was marked loss of axillary hair.

There was an almost mature cataract in the left eye and a very early lens change in the right eye.

During her stay in hospital she showed a peculiar mental state. She appeared depressed and gloomy. She had a perpetual frown on her face and did not converse with other patients. She answered questions in monosyllables.

Laboratory Studies

Haemoglobin 13·2 g.%. White cells 7,800 per c.mm. (differential count normal). Serum alkali reserve 47 vols.%. Chlorides (as NaCl) 540 mg.%. Sodium 333 mg.%. Potassium 14·3 mg.%. Chvostek and Trousseau signs. Vomiting and hiccough were Plasma proteins 6·5 g.%, (albumin 3·3 g., globulin 3·3 g., gamma-globulin 1·15 g.%). Blood urea 43 mg.%. Serum calcium 7·3 mg.%. Serum phosphorus 6·8 mg.%.

Urea clearance test—74% of normal function. Urinary concentration test—specific gravity up to 1022. Urine—N.A.D.; culture (catheter specimen)—no growth. P.S.P. excretion test—total excretion after 2 hours 4·4 mg. (73%). Ketosteroids—a 24-hour specimen of urine (2360 ml.) showed a total excretion of 4.5 mg. of 17 ketosteroids (estimated as dehydroandrosterone).

No clinical or laboratory evidence of moniliasis was found.

Radiological examination of the skull now showed a small area of calcification which had not been present on the patient's first admission. It was not in the region of the basal ganglia and probably represented a small area of calcification in the choroid plexus of the lateral ventricle.

An *electrocardiogram* again showed isoelectric T waves in leads V 4, 5, and 6. PR interval 0·16. Qt interval 0·37. QTc interval 0.45.

An *electroencephalogram* (Dr. C. Mundy-Castle) revealed abnormalities of isolated focal sharp waves or spikes from the left temporal region, together with left-sided bursts of 7-9 c/sec. from the same area. Occasional right-sided temporal sharp waves were also seen. Hyperventilation evoked several generalized paroxysmal bursts of 6-7 c/sec. activity, one burst of 4 c/sec. activity and several bursts of 24 c/sec. This response is of doubtful normality.

Ellsworth-Howard Test. This test demonstrated a marked increase in the excretion of urinary phosphorus following injection of parathormone (see Fig. 2).

Treatment

On 1 September treatment with A.T. 10 was commenced. Three ml. was given twice daily with remarkable effect. In 7 hours the Chvovstek and Trousseau signs had disappeared, and the Sulkowitch test became positive within 5 days.

The return of the blood calcium and phosphorus levels to normal confirmed the clinical improvement.

The patient now showed a marked improvement in her mental state. She became cheerful, co-operative and verbose and mingled freely with her fellow patients.

An electrocardiogram now showed a QT interval of 0·32 with T-wave inversion over V 5 and 6.

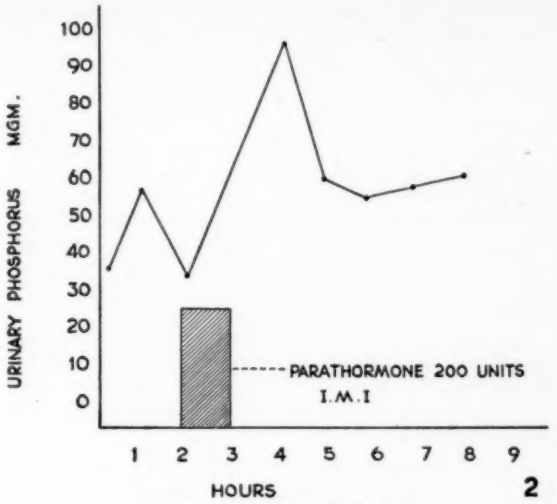

Fig. 2. Ellsworth-Howard Test.

Further, there was now no evidence of cardiac failure. She maintained her improvement as an out-patient on a maintenance dose of A.T. 10, the amount being based according to her requirements.

DISCUSSION

Etiology. Hypocalcaemic tetany may occur as a result of (1) deficient intake or absorption of calcium, (2) severe renal failure with phosphate retention and consequent reciprocal hypocalcaemia, or (3) hypoparathyroidism, usually due to operative removal of the parathyroid glands during thyroidectomy, or rarely idiopathic hypoparathyroidism.

This patient had an adequate intake and absorption of calcium as shown by absorption studies and stool examinations. Her renal function was moderately good and she had undergone no operation on the neck. Her repeated low blood-calcium and high blood-phosphorus reports, the ectodermal lesions, and her dramatic clinical and biochemical response to parathormone and A.T. 10, confirmed this as a case of idiopathic hypoparathyroidism.

The reason why all 4 parathyroid glands should cease to function is unknown. Sutphin, Albright and McCune[9] in 1943 reported 5 cases of idiopathic hypoparathyroidism associated with moniliasis. This may be purely coincidental or may be due to a predisposition of one disease for the other. It is interesting that Talbot, Butler and MacLachlan[10] in 1943 described 2 cases of moniliasis associated with Addison's disease; in one of them hypoparathyroidism was co-existent. The association of Addison's disease and idiopathic hypoparathyroidism has been noted by several observers and in 1946 was reviewed by Leonard,[8] who presented the clinical history and autopsy findings of one such case.

Albright *et al.*[1] in 1942 first reported 3 cases of an interesting condition which they termed 'pseudo-hypoparathyroidism—an example of Seabright-Bantam syn-

drome'. In this condition there may be a normal secretion of the hormone but the organism fails to respond. In addition this syndrome has certain developmental abnormalities, e.g. short stature, round facies and short fingers, which serve to differentiate it from true hypoparathyroidism. Ellsworth and Howard [4] in 1934 devised a test which may be used to differentiate these two conditions. This test is based on the fact that in true hypoparathyroidism the first metabolic change to occur after the administration of parathormone is an increased excretion of phosphate in the urine; no such response occurs in pseudo-hypoparathyroidism. In our patient the test was positive, indicating true hypoparathyroidism (Fig. 2).

The association of hypertension in this case was probably coincidental. The hypertension was regarded as essential in type and it is noted that her cardiac failure responded to bed rest and the therapy for hypoparathyroidism.

Symptomatology: de Mowbray [2] in his recent analysis of 57 cases listed the chief ways in which hypoparathyroidism may present as follows:

	Number of Cases	*Percentage*
Tetany	40	70
Epilepsy or generalized convulsions ..	24	42
Laryngeal spasm	5	9
Ectodermal lesions	6	11
Failing vision due to cataracts ..	6	11

This case presents the majority of the classical features. Signs worthy of note were the marked manifestations of tetany, including hiccough and vomiting probably due to spasm of the diaphragm and pylorus respectively. On the first admission no ectodermal lesions were noted, but with the patient's failure to attend regularly as an out-patient over a period of 2½ years these ectodermal lesions appeared and were then a marked feature. Presumably the maintenance of correct out-patient therapy will prevent the progression of these lesions and possibly a regression. Learner and Brown [7] reported a case of extreme trophic changes in a patient with hypoparathyroidism; these changes appeared to have a seasonal incidence, appearing in January (winter) and disappearing in June (summer); on dihydrotachysterol therapy the tetany, ectodermal lesions, cheilitis and glossitis all disappeared, the loss of vision was arrested and no further loss of hair occurred.

The mental state of our patient is worthy of emphasis. On admission her depression and antagonism was striking. With the restoration of the serum calcium to normal levels she became cheerful, co-operative and sociable. Greene and Swanson [6] report similar symptoms. They list anxiety, depression, a sense of impending disaster and, in severe cases, delusions and hallucinations. Even suicide may be attempted. They report the prognosis as being good and recovery following the maintenance of a normal blood calcium level.

Radiology. Calcification in the basal ganglia and cerebellum occurs quite commonly in cases of hypoparathyroidism. In this case no such calcification was noted. However, a small area of calcification appeared in the choroid plexus of the lateral ventricle which had not been there on the first admission.

Electrocardiography. The prolongation of the QT interval which was observed may occur in tetany from any other cause.

Electroencephalography. Gotta and Odoriz (1948) [5] describe (*a*) groups of abnormally slow waves, sometimes alternating with normal rhythm; (*b*) spikes; or (*c*) typical epileptic changes. This case showed abnormalities of focal sharp waves or spikes from the left temporal region.

Treatment. Parathormone is not used in the treatment of hypoparathyroidism. Its chief disadvantages are that owing to the fact that it is a foreign protein it leads to antihormone formation and resistance in the patient. It may give rise to reactions. (In this patient an intradermal injection of one minim of parathormone resulted in a moderate-sized wheal. The Ellsworth-Howard test had therefore to be modified; instead of 200 units of parathormone being injected intravenously, the same dose was given intramuscarly over the period of one hour.) Parathormone is also expensive and has to be given by injection.

Dihydrotachysterol (A.T. 10) is very effective for this condition. It is relatively inexpensive, it is taken by mouth, and it is easy to control.

The Sulkowitch reaction is a rough guide to treatment and is easy for patients to carry out on their own. However it is not an absolutely reliable guide, and regular blood calcium and phosphorus estimations should be carried out.

SUMMARY

1. A case of idiopathic hypoparathyroidism is described.

2. A brief summary of this clinical entity is given.

We should like to express our thanks to Dr. C. Mundy-Castle for the electroencephalographic report and to the South African Institute for Medical Research for the numerous laboratory investigations; also to Dr. V. D. Gordon, Superintendent of Coronation Hospital, for permission to publish this report.

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THE RADICAL CURE OF URETHRAL STRICTURES

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Until recently the accepted treatment of urethral strictures was dilatation with bougies or metal sounds. Operative measures were not invoked until palliative treatment failed owing to the type of stricture or because the patient did not attend regularly.

Although it is still consistently stated that dilatation should be a painless procedure, it is difficult to understand how this can be so in certain cases. If the stricture, whatever its length, is fibrous and relatively unyielding then painless dilatation is impossible. Local surface anaesthesia cannot penetrate the fibrous scar tissue to reach the sensitive nerve endings; it affects only the urethral mucosa, and it is reasonable to conclude that stretching of a fibrous stricture with its embedded nerve endings must be painful. With the yielding and elastic stricture the position is different, since the scar tissue is not so dense and the nerve endings may be successfully anaesthetized but, on the other hand, this is the type which rapidly attains its previous diameter and surgical interference becomes inevitable. When once a reasonable passage is obtained, dilatation is no longer necessary and one has merely to test the calibre from time to time. Should narrowing recur, the patient has once again to undergo a painful procedure with frequent accompaniments of catheter fever, bacteraemia and other complications.

In the author's experience the finding of an uncomplicated urethral stricture at the out-patient department of the Provincial Hospital, Port Elizabeth, is extremely uncommon. The patients usually present with badly neglected or improperly treated lesions, including cases of failed dilatation with multiple false passages and cases presenting with a low suprapubic cystostomy. With persistent and careful dilatation, commencing usually with a filiform guide and Phillips' catheter, it has been possible in most cases to produce a passage of reasonable diameter, only to find that the patient then disappears for some months and usually does not attend again until these complications are again present. The final outcome of treatment under these circumstances is usually disappointing and it was because of this that the author considered radical surgery might provide the best means of permanent cure. Robinson [1] states: 'The patient with stricture is never cured and it must be impressed upon him that regular, even if infrequent, passage of an instrument is essential to ward off serious trouble. Prognosis is relatively bad if gross sepsis has occurred before treatment is initiated or if it persists in spite of treatment.'

Until very recently text-book descriptions of surgical procedures in urethral strictures were those devised many years ago. Wheelhouse's classic external urethrotomy and the surgical instruments he used were described in 1876,[2] since when there had possibly been minor changes in technique and improvements in methods of drainage but no real advance in knowledge. All methods adopted were liable to produce further scar tissue and recurrence of the stricture. It makes little difference whether one totally excises the stricture, opens its floor, or incises its roof as in internal urethrotomy. Continued dilatation is advised after all these procedures. Statistics of local cases of stricture in which surgical intervention has been necessary are not available, but it is common experience that when once the older surgical procedures were carried out a vicious circle was set up, since almost invariably repeated operations followed by dilatation became necessary, particularly in the presence of complications.

THE DENNIS BROWNE TECHNIQUE

The introduction by Dennis Browne[3] of his highly successful operation for the treatment of hypospadias in children was soon followed by the application of his method to the radical cure of urethral stricture. Results have been published by Bonnin [4] and Swinney.[5] Although techniques differ on minor points, and in Johansen's operation [6] there is greater variation in his use of scrotal skin, these reports have shown a great improvement on previous results.

The basis of the operation is the formation of an interrupted length of hypospadic urethra which includes the area of the stricture. The length of urethra involved depends on the length of the stricture and partially on its position. In the penile and perineal sections the distance exposed may be minimal, since the skin and urethra when incised lie on adjacent planes or can easily be brought into juxtaposition. On the other hand, in the scrotal and membranous parts I have found it necessary to expose and lay open a greater length; in earlier cases a minimal length of urethra was opened, which led to the formation of a fistulous tract rather than the open gutter of a hypospadias, and closure at the second stage was difficult although results have been satisfactory. Careful attention has been given to the preservation of all mucosa. The second stage, done 4-6 weeks later, consists in burying the strip of mucosa and skin to give a lumen of about 0·8 cm. diameter to the new urethra. This requires a strip 2·5 cm. (1 inch) in width. I have used rubber tubing instead of the beads recommended by Dennis Browne [3] to obtain eversion of the edges. Latterly, I have been using large Michel clips as reported by Swinney.[5] I am also coming round to the idea that diversion of urine is unnecessary until the second stage unless infection is present, when a suprapubic cystostomy should be performed immediately.

My experiences have convinced me that radical surgery with the intention of permanent cure of urethral stricture is the treatment of choice.

The following case reports show the different methods used, in the various types of complicated or uncomplicated strictures, depending on their site.

CASE REPORTS

Penile Shaft Strictures

The skin and urethra are incised on a metal sound distal to the stricture for ½ inch. The stricture is cut through and the incision is lengthened proximally to the stricture for ½ inch. Gross bleeding points are clipped and tied off with 00 plain catgut. The urethral cut edge is sutured to the skin edge with Deknatil. A urethral catheter is inserted through the proximal opening and left for a few days. When the catheter is removed the patient passes urine through the gutter. Four to six weeks later the hypospadias is closed according to the method of Dennis Browne. Here an extensive relieving incision, which may leave half of the penis uncovered, is necessary on the dorsum of the penis. Epithelium grows over this area very quickly, leaving a soft pliable scar. Urinary diversion is effected by perineal urethrostomy.

Case 1. A Coloured taxi-driver aged 53 years. This patient gave a history that a partial amputation of the penis had been performed on him 6 years previously. This was followed by a meatal stricture. Repeated dilatation of the latter caused damage to the anterior urethra, resulting in a stricture of the entire urethra of the penile shaft. He was treated surgically at another urological centre but the stricture recurred and he had been receiving dilatations intermittently for some years. When an adequate calibre had been obtained, he invariably disappeared for some months, during which period he dilated himself with knitting needles. On his reappearance, I invariably had to start with filiforms.

He was operated upon over one year ago. His urethra accommodates a 20 French bougie and he has not required dilatation since operation. He carries on his normal work.

Case 2. A Coloured labourer aged 43 years. This man gave a prolonged history of stricture and he was passing most of his urine through a pin-head fistula on the side of the shaft. Micturition took about 10 minutes. Dilatation has been performed elsewhere and was attempted in the out-patient department without success.

The stricture was exposed and treated as above described. At the first stage the fistulous tract was completely excised. A second unsuspected stricture was found in the perineal portion and treated as in case 4. A small fistula on the shaft recurred after the second stage. This closed satisfactorily after surgery. The urethra now takes a 20 French panendoscope without difficulty. Dilatation has not been necessary.

Scrotal Urethral Strictures

Exposure of these strictures is obtained in the usual manner but the incision should extend on to the penile shaft and back to the perineum. If only a short length is exposed and the cut edges sewn to the scrotal skin, the effect will be to create a fistulous-like tract once the scrotum adopts its normal hanging position, and the final result a stricture where the distal part of the urethra is sewn to the scrotum.

Case 3. A Native labourer aged 70. This man had received dilatations intermittently over many years. The stricture was slowly narrowing and finally retention occurred. At operation, a short by-pass false passage was found skirting the stricture. This had been the object of the previous dilatations. When the stricture was incised the resulting width of the mucosa was only 2 mm. Only a short length was exposed and sewn to the scrotum. A stricture developed at the distal part of the urethra. A second operation splitting the scrotum was performed with complete success. The new urethra now takes a 26 French bougie.

Perineal Urethral Strictures

These if uncomplicated lend themselves very well to operation. The procedure carried out is similar to that of strictures of the shaft, but no relieving incisions are necessary.

Case 4. A European ex-serviceman. This man's original stricture followed the accidental use of chromic acid as a urethral douche. He had had previous surgical treatment elsewhere and now required dilatation every 6 weeks. These dilatations were painful and there was no increase in calibre. Routine reconstruction was done and when last seen the urethra accommodated a 19 French bougie.

Watering Can Perineum

In these cases all urethral surgery is preceded by suprapubic diversion of urine. In cases with extensive and numerous fistulae I now make an inverted-Y incision. The vertical incision can be extended to split the scrotum; I have frequently found a fistulous tract running up to the area of the symphysis pubis behind the scrotum, invariably on the left side. The arms of the Y extend in a curved line to the sides of the anus. All scar tissue must be excised and skin edges of fistulae trimmed. In view of the possible difficulty in freeing the perineal skin at a second stage, I use the scrotum to create the gutter in the manner described by Johansen. The second stage is done in the usual fashion.

Case 5. A Native labourer aged 52 years. This man gave a long history of repeated perineal abscesses with continual leakage of urine. Operation was carried out as above described but it was impossible to sew the scrotum on to the urethra as advised by Johansen. A second stage was uncomplicated. The urethra takes a 24 French bougie with ease.

Case 6. A European aged 59 years. This man gave a history extending over 20 years, with multiple abscesses and sinuses. For the last year he had been unable to sit comfortably; he walked with a stoop and with his legs apart to avoid contact with his trousers and had lost about 30 lb. in weight. He had been treated surgically in another urological centre. An inverted-Y incision was made, but it was found impossible to remove all the tracts and scar tissue through this. There were 2 large tracts running up on each side of the shaft, which required splitting of the scrotum and its subsequent reconstruction. Finally an area of skin 6 by 4 inches was excised. This extended well on to both thighs and posteriorly past the right side of the anus, completely denuding the perineum. The underlying scar tissue was excised and when this was completed the two crurae were seen to be stripped and the urethra, denuded of its muscle and cavernous tissue, was bulging. On passing a sound it was now found that the urethra would take a 24 French. Nothing further was done and the wound was allowed to granulate over. The patient had to return to the theatre 2 weeks later for drainage of a small abscess which formed at the base of the penis where the scrotum was reconstructed. He now takes a 20 French without discomfort. During his stay in hospital he regained 20 lb. in weight and now walks upright and can sit on a hard chair. This case is reported to show the importance of full excision of scar tissue; here the narrowing of the urethra was entirely due to extra-mural compression.

Membranous Urethral Strictures

In these cases I have closely followed the method of Johansen with good results. Owing to the depth and relative fixity of this part of the urethra I have found that it is difficult to get the posterior and more proximal sutures to hold if perineal skin is used. A lengthy gutter should be made which comes well forward into the perineum and allows easy secondary closure.

Case 7. A Native labourer aged 55 years. This man had been dilated intermittently for a stricture proximal to the bulb. His attendances were spasmodic; he finally arrived with retention and a cystostomy was performed. The only point of difficulty was

finding the entrance to the stricture. In other areas it is always possible to find the proximal urethra and so demonstrate the stricture, but in the membranous area this is impossible and a sound passed distally from above through a suprapubic cystostomy may be necessary. Closure was satisfactory and the patient takes an 18 French Coude bougie.

Case 8. A European youth aged 14 years. In this case I was unable to bring the skin back into contact with the urethra. Instead the urethra was allowed to reform around a catheter. The inevitable infection caused stricture formation. This boy had been run over by a lorry and suffered a complete tear of the urethra at the apex of the prostate together with other multiple injuries. At operation, elsewhere, they had managed to introduce a Jacques catheter, but no effort was made to approximate the bladder and prostate to the triangular ligament. It says much for the initial treatment that the boy shows no other disability than a urethral stricture.

When the catheter was removed, retention recurred and a suprapubic cystostomy was performed. At a subsequent operation an approach from the perineum was unsuccessful. Rectally, the whole area was one mass of scar and fibrous tissue. This was so dense that a metal sound in the membranous urethra could not be felt per rectum. A second perineal approach was made. Extensive scar resection was necessary and finally a mucosal tract was found, leading to the apex of the prostate which, on a subsequent cystogram, was shown to be elevated about 2 cm. above what was left of the triangular ligament. It was found impossible to bring either perineal or scrotal skin down to this depth. The thin strip of mucosa was left lying open and a new urethra was allowed to form around a perineal catheter. This perineal urethrostomy opening was later allowed to close. This boy required regular dilatation, but when last seen could be easily dilated to a 22 French. Dennis Browne [7] makes mention of this attribute of mucosa and greater use should be made of it to fill gaps in urethral continuity once the urethra is marsupialized.

Bonnin [4] has described a somewhat similar case which he successfully treated by bringing skin down to the apex of the prostate, but a stricture formed.

An interesting feature of this case is the length of unsupported lax urethra lying between the triangular ligament and the apex of the prostate. If this boy tries to use pressure to micturate or if his bladder becomes overful, he immediately precipitates a retention. When a desire to micturate arises, he has to wait for urine to trickle into his lax length of urethra and fill it. Once this has happened, he can use as much force as he desires without interfering with the passage of urine. The only explanation I can offer is that this unsupported urethra kinks on pressure from above when empty but when full of urine becomes a semi-rigid tube.

If the stricture in this case becomes difficult to manage, it may be necessary to make another effort at radical cure when the perineal tissues have settled down.

Complications

In this series two small fistulae have formed where the everting stitches had been introduced. These were due to two factors: The first and most important was that the sutures were too tight and local ischaemia was caused; the second factor was the use of braided nylon as a suture material. I now use very fine mono-filament nylon. Only one of these fistulae required further operation.

Apart from two fine hairs seen in one case, no trouble has arisen from buried hair growth as reported by Bonnin [4] and suggested by Smith.[8] Perhaps the fact that the Bantu has a relatively hairless perineum, accounts for the absence of this complication.

Results

Apart from case 8, no patients have required dilatation after operation; the follow-up in some cases has been short but, as this is the usual finding after the repair, I do not anticipate that any narrowing will develop in the future.

No patients have complained of after-dribbling as reported by Johansen. This I attribute to two points: The first is that no strip more than 1 inch wide was buried. The second is minimal freeing of the surrounding skin at the second stage, which avoids an unnecessary dead space and prevents gaping of the buried strip edges; if gaping is present, the final calibre is much wider than required.

SUMMARY

The methods and results are reported in a selected series of cases operated on for stricture by the Dennis Browne technique of burying a strip of mucosa and skin.

The author's minor modifications of technique, used for different types and sites of stricture, are described.

The fact that cure and not temporary relief is the aim of the operation, is stressed.

I wish to thank Dr. J. McLean, Medical Superintendent of the Provincial Hospital, Port Elizabeth, for permission to publish these cases.

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ABSTRACT : UITTREKSEL

The Specificity of the Treponemal Immobilization Test. Henry E. Zellmann. November 1954. Amer. J. Syph., 38, 507.

This test designed to distinguish between syphilitic and biologic false positive reaction was performed on 596 patients, of whom 441 had syphilis and 110 a wide variety of disorders other than syphilis, and 45 were normal individuals, the latter group including physicians, secretaries and technicians. The tests were performed at the Johns Hopkins Medical School, Baltimore.

It was found that the test approached absolute specificity. Normal persons were negative in 99·7% of cases. It was not certain whether the 0·3% of reactors actually had syphilis or whether the error was technical. In untreated syphilitic infection the TPI test was positive in 64·9%, 96%, 100% and 93·2% of cases of primary, secondary, late symptomatic and congenital syphilis respectively.

The test gave positive results in the treponematoses other than syphilis. In treated early syphilis the TPI test becomes negative more slowly than other serologic tests. In treated late syphilis the TPI test persists indefinitely in at least 96% of cases.

F.W.F.P.

A TRUE HERMAPHRODITE

CASE REPORT

G. P. CHARLEWOOD, F.R.C.S.(ED.), F.R.C.O.G.
and
D. FRIEDBERG, M.B., B.CH. (RAND)
Coronation Hospital, Johannesburg

V.K., a Bantu 'female', aged 21, consulted her doctor to see if anything could be done about her genitalia, which at an early age she had noticed to be different from others. She was referred to Coronation Hospital.

Menstruation had commenced at 19, being a scanty loss for 2-3 days, with dysmenorrhoea, at rather irregular intervals. Intercourse had never occurred; the patient claimed to have had erections when sexually aroused by attractive females, but that more frequently she had female desires when stimulated by men.

On examination the patient was found to have the build of a lightly built male. The hair distribution was female. The breasts were fully developed as in the normal female.

The external genitalia consisted of a large phallus equivalent in size to that of a normal adult penis, lying in folds of skin corresponding to labia. A sulcus like that of hypospadias was present. Below the phallus was a small orifice through which the patient both urinated and menstruated. The anus was in the normal position (Fig. 1).

Fig. 1. External organs.

On rectal examination a small uterus was felt, with normal utero-sacral ligaments. Masses corresponding in size and position to normal ovaries were palpable. X-ray pelvimetry showed an android type of pelvis.

On 5 March 1954 a laparotomy revealed a small normally formed uterus with a small fibroid on it. The Fallopian tubes were normal.

The left gonad appeared to be a normal ovary, the right was larger than the left and was divided vertically into two portions by an obvious line of demarcation. The medial was somewhat larger than the lateral and appeared to be normal ovarian tissue, the lateral was of much softer consistency and of a greyish colour. It looked and felt like testicular tissue.

Biopsy specimens were taken from both gonads and from the skin of the phallus. They were reported upon by Dr. B. J. P. Becker, Professor of Pathology, University of Witwatersrand, as follows:

Sections of the gonad on the left side show the presence of normal ovarian tissue in which an old corpus luteum and an occasional simple follicular cyst has been observed (Fig. 2).

Sections of the gonad on the right side show the structure of an ovotestis. The *ovarian portion* of this shows the presence of a corpus luteum. The *testicular portion* shows the presence of well-developed seminiferous tubules, in which there is no evidence

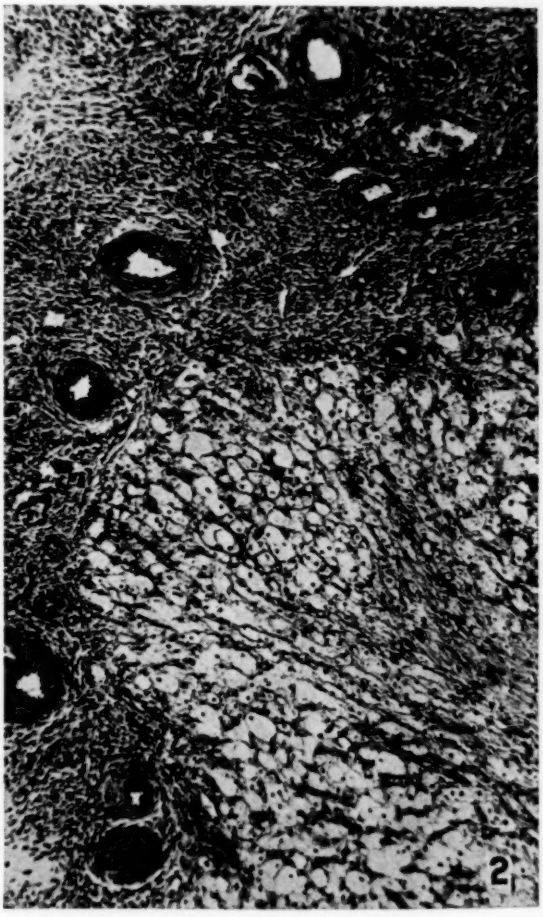

Fig. 2. Left ovary × 120. Section shows ovary and a portion of corpus luteum.

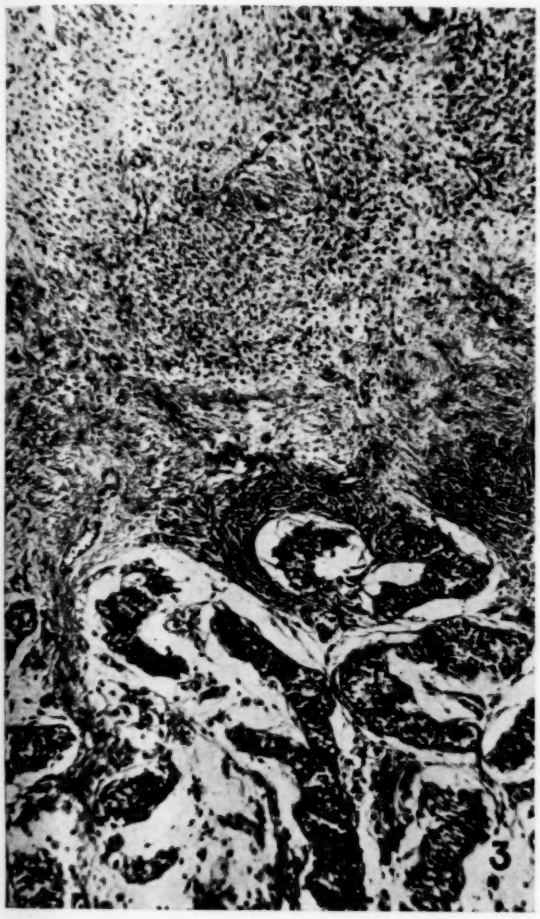

Fig. 3. Right ovotestis × 120. Section shows portions of ovarian and testicular tissue.

of spermatogenesis, and hyperplastic Leydig-cell tissue. The testicular portion is separated from the ovary by a fairly thick band of collagen. (Fig. 3.)

Sections of the skin show the structure of a *chromosomal* female.

On 26 March an operation was undertaken to modify the genitalia to the female pattern.

By means of probing it was established that the perineal orifice was a narrow vagina leading up to the cervix and that the urethra opened into it just within the entroitus. The perineum was slit posteriorly and the vagina was dilated up to the size of a No. 14 Hegar's dilator. A small nulliparous cervix was found in the vaginal vault.

The skin surface was stitched to the vaginal epithelium where the perineum had been divided, and a mould was left in the vagina for 1 week.

From the 10th day the vagina was dilated daily with glass dilators until a normal-sized vagina was obtained.

COMMENTARY

The term hermaphrodite is used to indicate that a person is bisexual in both the gonadal and secondary sex-structures. A true hermaphrodite, in the strictest sense, should be able to fertilize a female, be fertilized by a male, and fertilize itself, but no such case has ever been authoratively reported in man.

The term pseudo-hermaphrodite indicates that the person has gonads of one sex, and is bisexual in the secondary sex-structure.

True hermaphrodites can be classified as follows:

1. *Bilateral.* Testis and ovary (ovotestis) on both sides.
2. *Unilateral.* Ovotestis on one side with ovary or testis on the other side.
3. *Lateral or Alternating.* Testis on one side and ovary on the other side.

The case reported here belongs to the unilateral type with an ovotestis on the right side and a normal ovary on the left side.

The diagnosis of genetic sex of these persons cannot be made by inspection of the external genitalia. For absolute accuracy microscopic examination of the gonads is necessary. Inspection of the surface of the gonad is not sufficient and there are cases on record where mistakes have been made until thorough microscopic examination of the gonads has been carried out (Engle *et al.* 1946).

In the treatment of mature hermaphrodites and pseudo-hermaphrodites genetic sex plays a secondary role to psychologic sex (Ellis 1945, Young 1932). In this particular case the patient volunteered that her emotions were mainly those of a female, probably because of the well-developed breasts, smooth skin and facial characteristics. Because of this and also because of the development of uterus, cervix, and tubes it was decided to enlarge her vagina, to remove the large phallus, and to give her the external genital appearance of a female.

Reconstruction of the genitalia in pseudo- or true hermaphrodites should not include castration. The only indication for castration should be a pathological lesion of the gonads themselves. The development of malignant lesions in intra-abdominal testicles, although commoner than in scrotal testes, is still so rare that castration is not justified on these grounds alone. Removal of the gonads merely because they are opposed to the psychological sex will not change the emotions, but rather will take away from the patient hormonal influences that are beneficial (Brewer *et al.* 1952).

When the diagnosis of intersexualism is made at an early age it is important to establish the true sex by gonadal biopsy. This affords the opportunity of bringing up the child in its correct sex.

Detection of Chromosomal Sex in Hermaphrodites from Skin Biopsy. It has been found that the nature of the sex chromosomes (XX or XY) in an individual may be detected by examining the epidermal nuclei in a small biopsy of skin. This technique offers a new approach to the vexatious problem of hermaphrodites.

The nuclei of female specimens contain a mass of sex chromatin which is seldom seen in male specimens. The sex chromatin is believed to be derived from heterochromatic parts of the sex chromosomes. The XX

chromosomes of the female produce a chromatin mass sufficiently large to be identified, while the XY chromosomes of the male fail to produce a chromatin mass of sufficient size to be distinguished from the general particulate chromatin. (Moore *et al.* 1953, Broster *et al.* 1953).

The exact significance of chromosomal sex determination is not yet known.

The skins of the few true hermaphrodites so far examined and reported in the literature have shown the female skin structure, as in the case published here.

We are grateful to Dr. B. J. P. Becker for his interest and his histological report, to Dr. Dezulovick and Dr. F. Brandt for the photographs, and to Professor O. S. Heyns for his interest and encouragement.

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POLIOMYELITIS IN THE UNION

Following are the returns, supplied by the Union Department of Health, of cases notified under the Public Health Act as suffering from Poliomyelitis in the period 10 to 17 February 1955.

	European	*Non-European*
Transvaal:		
Johannesburg	7	
Johannesburg P.U.A.H.B.	2	
Pretoria	3	
Vereeniging P.U.A.H.B. (1 fatal)	2	1 (fatal)
Krugersdorp	1	
Brits	1	
Benoni	3	2
Amersfoort	2	
Amersfoort district	1	
Standerton district		1
Germiston	3	
Lichtenburg	1	
Boksburg	2	
Ventersdorp district		1
Klerksdorp		1
Brakpan	1	
Evaton		1
Total for Transvaal	29	7
Cape Province:		
Cape Town Div. Council	1	2
Peddie Mag. district		1
Barkly East Div. Council	1	
Beaufort West Div. Council	1	
Queenstown Mun.	1	
Mount Fletcher Mag. district		1
Caledon Div. Council	1	
Lusikisiki district		1
King William's Town Div. Council		1
Total for Cape Province	5	6
Natal:		
Durban	11	3
Pietermaritzburg	4	
Pietermaritzburg district		2
St. Michaels (on sea) (fatal)	1	
Camperdown district		2
Colenso	1	
Msinga district		1
Bergville		1
Ndwedwe district		1
Richmond		1
Illovo Beach	2	
Melmoth district		1
Baven (on sea)	1	
Inanda		1
Total for Natal	20	13
Orange Free State:		
Bloemfontein	1	1
Total for O.F.S.	1	1
TOTAL FOR THE UNION	**55**	**27**

PASSING EVENTS : IN DIE VERBYGAAN

Dr. I. Schrire, of 1 Hof Street, Gardens, Cape Town, left for England on the *Edinburgh Castle* on 25 February. He will be engaged on endocrine research in London for 1 year.

* * *

Dr. W. L. F. Hatchuel, M.B., Ch.B. (Rand), M.R.C.P. (Edin.), D.C.H. (R.C.P. & S. Eng.), is terug in Johannesburg na sy onlangse besoek aan die Verenigde Koninkryk.

Tydens sy verblyf aldaar het hy in Birmingham ageer as Registrateur aan die Sorrento-Instituut vir Vroeggebore Babas asook aan verwante afdelings vir Pasgebore kinders en Kindersiektes, en in Londen as Mediese Registrateur aan die Hospitaal vir Siek Kinders, Great Ormondstraat.

Hy praktiseer nou as algemene geneesheer by Princess Heights 11, Kotzestraat 86, Hillbrow, Johannesburg. Tel.: 44-9273 (Spreekkamer), 43-1222 (Woning).

* * *

Dr. W. L. F. Hatchuel, M.B., B.Ch. (Rand), M.R.C.P. (Edin.), D.C.H. (R.C.P. & S. Eng.), has returned to Johannesburg after his recent visit to the United Kingdom.

While there he worked as Registrar to the Sorrento Premature Baby Unit and allied neonatal and paediatric units in Birmingham, and as Medical Registrar in the Hospital for Sick Children, Great Ormond Street, London.

He has now opened rooms in general practice at 11, Princess Heights, 86 Kotze Street, Hillbrow, Johannesburg. Telephones: 44-9273 (rooms); 43-1222 (residence).

Royal College of Physicians of Edinburgh. At the quarterly meeting of the College held on 1 February 1955, the President Dr. L. S. P. Davidson being in the Chair, the following were amongst the persons who were elected Members of the College: J. A. Kay, M.B., B.Ch. (Rand), B. Kaplan, M.B., Ch.B. (Cape Town), E. D. Myers, M.B., Ch.B. (Cape Town), and C. G. Caro, B.Sc., M.B., B.Ch. (Rand).

* * *

Cape Town Paediatric Sub-Group. The Annual General Meeting of this Sub-Group was held on 2 February 1955 at Groote Schuur Hospital. The following office-bearers for the current year were appointed: *Chairman*—Dr. R. F. Maggs, *Vice-Chairman*—Dr. P. V. Suckling, *Hon. Secretary*—Dr. R. McDonald; *Committee members*—Prof. F. J. Ford, Dr. W. Emdin, Dr. I. Mirvish and Dr. P. M. Smythe.

The following clinical meetings were held during 1954:

9 April	Prof. F. J. Ford—*Infant Feeding.*
7 May	Cases presented at Groote Schuur Hospital by Drs. P. M. Smythe, J. Rabkin and E. B. D. Dowdle, and Messrs. J. H. Louw and A. Katz.
4 June	Film, *Asphyxia Neonatorum.*
6 August	Dr. N. v.d. Merwe—*School Medical Inspection.*
3 September	Dr. J. D. Hansen and Dr. P. V. Suckling—*Oedema in Kwashiorkor.*
1 October	Clinical Evening at Alexandra Institute.
12 November	Dr. W. P. U. Jackson—*Dwarfs.*
4 December	Dr. H. Phillips—*Social Aspects of Paediatrics.*

BOOK REVIEWS : BOEKRESENSIES

TRANSCENDENTALISM

Jaspers's Metaphysics. By A. Lichtigfeld, Dr. Jur., D.Phil. (Pp. 120 + xviii. 10s. 6d.) London: Colibri Press Ltd., 1954.

This work by Dr. Adolph Lichtigfeld is most welcome for two main reasons: firstly, because Karl Jaspers—that eminent Swiss philosopher—has exercised a great influence on theological thought; and secondly, because the English-speaking world will now be the richer for a deeper awareness of that influence.

Jaspers has concerned himself since 1932 with the principle of transcendentalism, and in the course of his speculations has recognized 3 possible modalities of transcending. The 1st consists in transcending the limits of empirical existence, with a view to putting the subjective activity of the Self into a position of infinite possibilities; the 2nd consists in illuminating empirical experience by our own individual subjective experience—which is a form of existential analysis; and the 3rd consists in the metaphysical act of cognition, which is directed to the equation of existence with ultimate reality.

In order to clarify the philosophic position of Jaspers, Lichtigfeld has written a necessarily ponderous introduction, but this, we fancy, will appeal in the main to readers who have some fundamental training in philosophy. The author, in order to indicate the evolution of Jaspers's philosophy, has most painstakingly catalogued the viewpoints of the earlier masters, but it would have been an advantage to the average reader if Lichtigfeld had rendered a more adequate and perspicuous synthesis of them. Students of philosophy will finally want to know: Has Jaspers given the answer to King David's interrogation: 'O, what is man that Thou art mindful of him, and the son of man that Thou heedest him?'?

We would say in all humility that Jaspers's answer misses the mark, in that it fails to take cognizance of that natural unity which the reviewer has designated 'the human continuum', and has represented by the notation: The Body-Mind-Spirit-Environment. Jaspers, by labouring under the influence of Berkley's pluralistic idealism, splits up this natural unity, and treats the parts as independent entities instead of segments which are functionally related to one another. Furthermore, he tends to regard the psyche as an independent variable occupying a place of dominance in the scheme of things; but in doing so he is virtually giving philosophic sanction to the age-old vogue of psychic escapism in a world of harrowing social realities which cry for solution. We hold rather with Dewey that the process of thought has no object outside of social experience, and no being of its own outside such experience. Thus, thinking is not a thing apart from perceiving, but the two are interactive, or mutually dependent. The process of thought, or ideation, is not an independent phenomenon, but is evoked by social situations; and in so far as it proves to be an effective instrument in dealing with the specific social situations by which it is evoked, it is true of those social situations.

We would break another lance with Jaspers and say that, as man is not only *homo psychologicus* but also *homo sociologicus*, the quality of his inter-personal relations in a given society must inevitably determine the quality of knowledge, and of truth. The truth of an idea is thus, correspondingly, a mark of its social acceptability. The mental processes productive of social truth constitute the processes of reason and express themselves in the rules of logic.

Finally we would urge that students of Jaspers, as elucidated by Lichtigfeld, would do well to appreciate the fine distinction between the terms 'truth' and 'reality'. Truth resides in the psyche, and is of necessity relative, fluid, and changeful, being contingent upon the body of knowledge obtaining at a particular time; but reality does not reside in the psyche, for it is not synonymous with experience; it is external to, and independent of, mental activity. This is the *coup de grâce* which neo-realistic philosophy, shaped by such thinkers as Meinong, Husserl, Russell, Whitehead, Moore and Alexander, has dealt to man's narcissistic egocentrism. It is, in our view, the answer to Jaspers's transcendentalism—a term, by the way, which was introduced by Kant, but subsequently deprecated by him.

L.F.F.

CHROMATOGRAPHY

British Medical Bulletin: Chromatography. Vol. 10, No. 3, 1954. Price 15s.

A few years ago medical men were somewhat vaguely aware of the use biochemists made of adsorption onto alumina and other inert solids in the preparation and purification of biological substances. They may have wondered, too, why it always seemed to retain what was wanted and to reject what was not wanted, or *vica versa.*

A few may have heard of Tswett who in 1910 passed a solution of chlorophyll through a column of finely powdered calcium carbonate and obtained a series of coloured bands as the different pigments passed down the column at differing speeds. Biochemists themselves were dilatory in exploiting this technique in the analysis of other mixtures of pigments; a process to which they gave the name of chromatography, and which has now been so vastly extended and applied to all sorts of substances, pigmented and colourless, organic and inorganic.

Dent's article in the *Lancet* (1946) on the separation of amino-acids in the urine by means of paper chromatography called the attention of most of us doctors to the possibilities of this new method in clinical medicine. Gordon, Martin, Synge and Consden (1943, 1944) had shown that paper could be used with advantage in the place of the column of magnesia, alumina or chalk as the stationary phase in the proceeding.

This had the advantage that very small quantities of material could be analysed very simply and the further advantage that a square of paper could be used first in one direction with one solvent and then in a direction at right angles to the first with another solvent. The result was that instead of a single row of spots some of which might overlap and be impossible to identify, there was a wide scattering of spots over the whole of a large sheet, and the possibility and certainty of identification were increased many times.

The increase in the applications of chromatographic methods in biochemistry in the last few years has been phenomenal. It has been applied to nearly all classes of substances of biological interest—amino-acids, peptides, sugars, porphyrins, antibiotics, steroids, inorganic ions. It can be used for preparative as well as for analytical work. Instead of relying on natural colours we now have a remarkable array of reagents for identification of the products, and these are reinforced by fluorescence or the quenching

of fluorescence, changes in surface tension, radio-activity and biological tests.

But a price has had to be paid for all this. The days of a drain pipe, a lead tray, a bit of paper and an amateur have gone, and we can soon expect a journal of chromatography, a journal of clinical chromatography, and the appointment of a full time chromatologist to all well-staffed hospitals.

How technical the subject has become can be gauged by reading the Chromatography number of the *British Medical Bulletin* published by the Medical Department of The British Council. The authors of the articles include many British pioneers whose names are familiar to all who have dabbled in chromatography: Martin, Williams, Consden, Partridge, Dent and many others. Between them they discuss very fully and helpfully the principles and applications of chromatography, and describe the methods and apparatus used for various purposes. Anyone without special experience who wishes to make use of these methods can hardly do better than start by consulting this collection of very valuable papers.

Gordon, A. H., Martin, A. J. P. and Synge, R. L. M. (1943): Biochem. J., **37**, Proc. xiii.

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G.C.L.

A TREATISE ON DERMATOLOGY

The Skin. By Arthur C. Allen, M.D. (Pp. 1048 + xv, with 495 illustrations. £10 12s. 6d.) St. Louis, U.S.A. C. V. Mosby Co. 1954.

Contents: 1. Embryology, Anatomy, and Physiology. 2. Definitions, Regional Distribution of Dermatoses, and Eponyms. 3. Histologically Identifiable Non-infectious Dermatoses. 4. Panniculitides. 5. Lupus Erythematosus, Dermatomyositis, Scleroderma, and Poikiloderma. 6. Lesions of Collagen and Elastic Tissue. 7. Dermatoses of Allergic Origin. 8. Vesicular Dermatoses. 9. Non-vesicular Virus and Rickettsial Diseases. 10. Pyodermas and Specific Bacterial Infections. 11. Tuberculosis, Sarcoidosis, Berylliosis, and Leprosy. 12. The Treponematoses and Nonspirochetal Venerial Diseases. 13. Mycoses. 14. Eruptions Caused by Protozoa, Arthropods, and Helminths. 15. Psychocutaneous Disorders and Miscellaneous Desquamative Dermatoses. 16. The Vitamins. 17. Vascular Disorders. 18. Abnormalities of Pigmentation. 19. Disorders of Cutaneous Appendages. 20. Non-Neoplastic Lesions of Oral Mucosa. 21. Classification of Tumors of the Skin. 22. Verrucae, Epithelial Cysts, and Tumors of Appendages. 23. Carcinomas of the Skin and Mucosa and Miscellaneous Tumors of the Oronasal Cavity. 24. Nevi and Malignant Melanomas. 25. Xanthomatoses and Lipid and Nonlipid Histiocytoses. 26. Tumors of Mesenchymal Tissues. 27. Tumors of Vessels. 28. Tumors of Hematopoietic Tissues.

This beautiful book is what the dermatological world has been waiting for. It is of great physical and intellectual dimensions, every page being packed with excellent photographs and invaluable descriptions of macroscopic and microscopic skin pathology. Unfortunately, apart from the frontispiece, there are no coloured photographs, always so particularly helpful in dermatology, but, no doubt, the inclusion of these would have made the price totally prohibitive.

'The Skin' is a clinico-pathologic treatise and the author achieves magnificently what he sets out to accomplish, a work which is a happy combination of clinical and histological dermatology. He makes it abundantly clear that 'the old order changeth, yielding place to new' wherein the modern physician no longer regards dermatology as the isolated step-sister of general medicine but looks upon the skin as the mirror not only of the mind but of countless pathological processes in the body as a whole. In his preface he states that 'it would seem that the capacity to study disease as a whole, rather than in artificially broken segments, should continue to comprise one of the great pedagogic aims in medicine' and, in his discussion on disseminated lupus erythematosus, he remarks that the observation of the L.E. phenomenon by Hargraves, Haserick and others 'is undoubtedly one of the most provocative discoveries in the field of cutaneous-visceral integration'. He hopes to implement 'a long-neglected interest in this enormously important organ of the body (the skin) which previously has been almost completely disregarded in books on general pathology'.

Professor Allen is generous with his references, there are more than two thousand of them. Modern concepts are clarified and the profuse nomenclature of dermatology is pared down to the simplest possible proportions. A long list of dermatologic eponyms is given. His classification of cutaneous manifestations of morbid processes is most acceptable. It savours of the unexpected, however, to find porphyria amongst the allergies, presumably because of the alleged element of photosensitivity in its etiology, instead of in the later section on inborn errors of metabolism. Unusual, too, is the pride of place given to lupus erythematosus, dermatomyositis and scleroderma, which have a chapter to themselves just *preceding* 'Lesions of Collagen and Elastic Tissue'. The reason for this is that the author considers that neither disseminated lupus erythematosus nor dermatomyositis is a diffuse vascular disease or a generalized disease of collagen.

If a dermato-pathologist as omniscient as Professor Allen can be said to have specialized, it is patent from his superb writings on neoplasms of the skin that these have held his interest for many years.

The latest modes of therapy are outlined, although the author does not profess to give details of treatment. Once the diagnosis has been made, on clinical and histological grounds, it is easy enough to find the best form of treatment minutely described in other works.

This treatise is not a *vade mecum* or simple handbook for those who are mildly interested in dermatology but a sound book of reference for teachers and post-graduate students of dermatology, pathology, medicine and surgery. No medical library will be complete without it.

J.W.

RABIES

Rabies. Bulletin of the World Health Organization, Vol. 10, No. 5, 1954. (Pp. 703-866. 10s.) Geneva: World Health Organization. 1954.

Contents: Part I. Virus Research. 1. Biological Modification of Rabies as a Result of its Adaptation to Chicks and Developing Chick Embryos.

Part II. Control of Rabies in Animals. 2. Experimental Studies on the Duration of Immunity in Dogs Vaccinated against Rabies. 3. The Control of Rabies in Malaya through Compulsory Mass Vaccination of Dogs. 4. A Field Demonstration of Rabies Control Using Chicken-Embryo Vaccine in Dogs. 5. Ecology of Rabies in Southern Rhodesia. 6. La Rage et sa Prophylaxie et Autriche. 7. Rabies in Canada, with Special Reference to Wildlife Reservoirs. 8. Transmission of Rabies by Bats in Latin America.

Part III. Prevention of Human Rabies. 9. Antiserum in the Prophylaxis of Rabies. 10. Phenolized Vaccine Treatment of People Exposed to Rabies in Southern India. 11. Prevention of Human Rabies: Treatment of Persons Bitten by Rabid Wolves in Iran. 12. Treatment of Wounds Inflicted by Rabid Animals. 13. Recent Advances in the Preparation of Antirabies Vaccine Containing Inactivated Virus. 14. Avianized Rabies Virus in Man. 15. Experimental Allergic Encephalitis in Animals, and its Bearing upon the Etiology of Neuroparalytic Accidents Following Antirabies Treatment in Man. 16. Can Man be Protected against Rabies?

This is another most valuable bulletin in a valuable series of bulletins issued by the World Health Organization. This publication gives a picture of recent developments in the field of rabies, particularly in the methods for its control.

Rabies is a disease which has been endemic for many years in the Orange Free State, the South Western Transvaal and the North Western Cape Province. In this region of South Africa it affects particularly the yellow mongoose or rooi meerkat *Cynictis penicillata*, which has been responsible for most infections in man. Within the last 5 years, however, the introduction of canine rabies across the Limpopo and its spread in the Northern and Eastern Transvaal has greatly increased the problem confronting the medical and veterinary authorities of this country. This bulletin is therefore of timely interest in South Africa and also in a number of other countries, notably Canada where, too, rabies has assumed greatly increased importance within the last few years.

Dr. Hilary Koprowski describes his studies, indicating that living chick-embryo-adapted virus can be used both as a vaccine administered before exposure to rabies virus and as an adjunct to antiserum in the protective treatment of animals after exposure.

Dr. Harald Johnson of the Rockefeller Foundation discusses the relative value of phenolized vaccine and the Flury strain of live virus and notes that the immunity conferred by the latter is superior.

The methods adopted for the control of rabies in Malaya, Israel, and Southern Rhodesia are described in detail. The description of the ecology of rabies in Southern Rhodesia by Dr. J. S. Adamson will be of particular interest to South African readers, especially his conclusion that the use of the Flury-strain avianized vaccine is satisfactorily controlling the disease in most of the areas involved.

The value of antiserum in the prophylaxis of rabies is discussed by Dr. K. Habel, and he concludes it has a definite place in the treatment of patients who have suffered severe exposure. The value of phenolized vaccine in the treatment of people exposed to rabies in India is analyzed by Dr. Veeraraghavan.

The methods of treating wounds inflicted by rabid animals are described in detail by competent authorities.

The methods of preparing rabies vaccine and the dangers associated with its administration are discussed, and finally Dr. K. F. Meyer summarizes the present position of this historic disease and concludes that rabies is a preventable disease and that all present-day scientific and administrative knowledge must be marshalled to erase the blot on 20th century civilization, which the continued prevalence of rabies constitutes.

J.G.

CHEMOTHERAPY—ANTIBIOTICS

Recent Advances in Chemotherapy. Vol. III. Antibiotics. By F. C. O. Valentine, F.R.C.P., and R. A. Shooter, M.A., M.D. (Pp. 292 + viii. Third Edition. 27s. 6d.) London: J. and A. Churchill Ltd. 1954.

Contents: 1. Penicillin. 2. Drugs Used in the Treatment of Tuberculosis. 3. The Tetracyclines, Aureomycin and Terramycin. 4. Chloramphenicol. 5. Bacitracin, Polymyxin, Erythromycin and Carbomycin. 6. Resistance. 7. General Principles. 8. Staphylococcal Infection. 9. Streptococcal and other Infections of the Upper Respiratory Tract. 10. Infections of the Lung. 11. Bacterial Endocarditis. 12. Tuberculosis. 13. Acute Meningitis. 14. Enteric Fever, Bacillary Dysentery, Infantile Gastro-Enteritis, Pre-Operative Suppression of Bowel Organisms, Peritonitis. 15. Urinary Infections. 16. Actinomycosis, Anthrax, Tetanus, Gas Gangrene, Erythema Serpens. 17. Venereal Diseases. 18. Spirochaetal Diseases other than Syphilis. 19. Brucellosis, Tularaemia and Plague. 20. Infections with Rickettsia and Viruses. Index.

Previous editions of this series were prepared by the late G. M. Findlay, who at the time of his death in 1952 had made considerable progress with the preparation of the present volume. F. C. O. Valentine and R. A. Shooter have now completed the work and in doing so have successfully summarized the modern methods of treatment of the bacterial, rickettsial and virus diseases amenable to antibiotic therapy.

From the index it can be seen that the authors have covered a very wide field, with a bibliography at the end of each section enumerating the most important papers of the last 5 or 6 years. In addition to a careful analysis of the various methods of antibiotic therapy they have presented much useful advice about the choice of drug, dosage and route of administration, and where doubt exists they have not hesitated to say so. Each chapter is most readable, and at the same time the subject headings are so arranged as to make details of information readily available for reference purposes.

The authors have succeeded in producing a well balanced guide to the most recent information on antibiotic therapy for the physician.

A.K.

BOOK ABOUT BREAD

Bread. By Lord Horder, G.C.V.O., M.D., F.R.C.P., Sir Charles Dodds, M.V.O., M.D., D.Sc., Hon. Sc.D. (Camb.), F.R.S. and T. Moran, C.B.E., D.Sc., Ph.D. (Pp. 185 with 20 illustrations. 18s.) London: Constable & Company, Ltd., 1954.

Contents: 1. The History of Bread. 2. The Wheats of the World. 3. The Chemistry of Wheat, Flour and Bread. 4. The Main Features of the Milling and Baking Processes. 5. Improving Agents. 6 The Digestion and Assimilation of Bread. 7. Bread and Nutrition. 8. The Enrichment of Flour and Bread. 9. Bread and Health. Conclusions. Index.

One realizes, after a perusal of this interesting book, that our scientific knowledge of flour and bread is now quite advanced. A great deal of this advance occurred during the recent war, when such restrictive measures as alterations in the extraction rate of flour were introduced. It was then found that much less was known than was realized about the implications of such a simple step, and this led on to research into the distribution of vitamins, mineral salts etc., in different parts of the wheat grain.

The phytic acid controversy was another practical problem which arose at this stage and resulted in the addition of chalk to flour in England.

These and many other investigations as well as the history of milling, milling processes and the place of bread in nutrition, are described in detail.

This book, as the authors say, is not for the specialist research worker, who would find it elementary, but for the doctor, science teacher, social worker and dietetician. To these we can wholeheartedly recommend it.

J.T.I.

CORRESPONDENCE : BRIEWERUBRIEK

THE EFFECT OF MELADININ IN THE TREATMENT OF VITILIGO

To the Editor : With reference to the article[1] on this subject in your Journal of 12 February. I wish to state that I used to treat this condition with the local application of 10% oil of bergamot followed by irradation with ultra-violet rays and, though most of the lesions responded to this therapy, unfortunately there were usually remissions which showed involvements more extensive than the original lesions. Therefore I discontinued and advised against this form of therapy.

Thus I read the paper on the results obtained with Meladinin plus ultra-violet light with great interest and take this opportunity to congratulate the authors. I hope that now we can help the many sufferers from this unsightly condition with its concomitant psychogenic disturbances.

R. Robins-Browne

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Johannesburg
21 February 1955

1. Schulze B. V. and Leeming, J. (1955): S. Afr. Med. J., **29,** 147.

TUBERCULOUS MENINGITIS

To the Editor: We should like to enter into the discussion between Dr. Craig[1] and Dr. Sonnenberg[2] on the treatment of patients with tuberculous meningitis.

1. It is obvious, to us at least, why Dr. Craig, as a busy general practitioner, is unable to carry out intrathecal treatment. In spite of the references quoted by Dr. Sonnenberg, there is much in the literature[3] to support treatment without intrathecal streptomycin.

2. On the use of ACTH Dr. Sonnenberg has misquoted his reference. Dr. Lorber's letter to the British Medical Journal[4] does not show 'that it is extremely doubtful if any benefits can be claimed for the use of ACTH in the treatment of tuberculous meningitis': but only that Dr. Bulkeley[5] had not proved its value in her article in a previous issue. We have observed a moribund child of 3 years who developed tuberculous meningitis while on streptomycin, PAS and INH, and who came to life and survived when ACTH was added. From this and several other cases we have gained the impression that ACTH will certainly be a useful drug in tuberculous meningitis, though the precise indications have still to be worked out.

ACTH may promote the spread of pulmonary tuberculosis: it promotes the spread of any infection. Such spread, however, can usually be controlled by antibiotics, and it should be understood that this is why ACTH can be used at all in infections.

3. It is true that Dr. Craig has given us inadequate details and a short follow-up of his cases but, still, his record of 8 patients still alive out of 8 can hardly be bettered, as far as it goes.

Dr. Craig is criticized for his short period of hospitalization. He mentioned in his article the resistance of the rural African to hospitalization. We have the additional problem, in Alexandra, of not being able to find hospital beds at all for our patients with tuberculous meningitis. We are forced to treat most of our patients in their homes. In our circumstances, and I am sure in Dr. Craig's

too, intrathecal streptomycin is an impossibility, and more patients can be saved by modifying a system of therapy than by waiting for a bed in a well-staffed hospital ward. We all agree with Dr. Sonnenberg that early diagnosis is essential, but only because lives are saved by early institution of treatment.

When treating tuberculosis in South Africa, one has to appreciate that the problem is mainly outside the scope of infectious disease hospitals. The main attack must be made by general practitioners, District Surgeons and clinics, and treatment has to be modified to suit the circumstances. Intramuscular injections and oral therapy are possible, for instance, in the domiciliary practice conducted by our Clinic. Intrathecal injections are not. One has to cut one's coat according to the cloth.

Mervyn Susser
Zena Stein
Margaret Cormack
Michael Hathorn

Alexandra Clinic
P.O. Bergvlei
Johannesburg
13 February, 1955

1. Craig, C. J. T. (1955): S. Afr. Med. J., **29**, 62 (15 January).
2. Sonnenberg, J. (1955): *Ibid.*, **29**, 144 (5 February).
3. Tuberc. Index (1954): **9**, 546, 556, 559, 572.
4. Lorber, J. (1953): Brit. Med. J., **2**, 1433.
5. Bulkeley, W. C. M. (1953): *Ibid.*, **2**, 1127.

NERVOUS BREAKDOWN AND HYPNOTISM

To the Editor: Although Dr. Z. Wolf's article on *The Nervous Breakdown*[1] proved interesting reading, I do not think that his method is the ideal approach for the general practitioner, as it is so time-consuming.

Today we have to develop methods which will bring some measure of relief in a shorter period of time, since psychoneurotic disturbances are so widespread.

The classical procedure of psycho-analysis takes many, many hours—even years. The results are unpredictable and there is no simple correlation between therapeutic results and the duration and intensity of treatment.

Used properly, and with the co-operation of the individual, hypnosis is one of the most powerful and beneficial psychological tools known to man. It can, in some cases, accomplish results which have the appearance of miracles. It is such results that have been too much stressed in the past, while little or no attention has been given to what hypnotherapy can do for the average individual.

S. Kaimowitz

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19 February 1955

1. Wolf, Z. (1955): S. Afr. Med. J., **29**, 157.

THE INDICATIONS FOR CAESAREAN SECTION

To the Editor: I should like to thank Professor James Louw for his very comprehensive and clear article which appeared in the *Journal* under this title.[1]

A few interesting points arise. I agree that the most unsatisfactory indication is foetal distress. Ideally, the operation should be performed for the cause of the foetal distress rather than for the foetal distress *per se*. However, sometimes a cause is not found either pre-operatively or post-operatively. Professor Louw's Department is to be congratulated on the fact that foetal distress is given as the indication for the operation in only 10 cases out of the total of 648 cases of Caesarean section. I presume that in these 10 cases no other cause was found. It shows a thorough investigation into the Caesarean section rate and is an example to follow.

I have had humiliating but happy experiences when working with Bantu patients. I have advised a Caesarean section for foetal distress as assessed by the criteria that Professor Louw outlines but where no other cause was found. Operation was refused and a normal healthy baby has been born (on one occasion 12 hours later), the patient having had coramine, synkavit and oxygen in the meantime.

In these cases, the placenta should be assessed microscopically as well as macroscopically. Most obstetricians have had cases with a history of repeated foetal deaths just before or during labour, and in which a Caesarean section at 37—38 weeks has produced a live and healthy child.

I agree with the author that the place of Caesarean section in accidential haemorrhage has not yet been finalized. There is the danger of its too frequent employment in cases that could be dealt with satisfactorily by vaginal delivery, especially as data about afibrinogenaemia and anuria is accumulating.

James Miller

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18 February 1955

1. Louw, J. T. (1955): S. Afr. Med. J., **29**, 160 (12 February).

GASTRIC DIVERTICULA

To the Editor: Dr. Price has written an interesting account of 2 unusual cases of gastric diverticula*. There are, however, a few facts concerning this condition which require further emphasis.

In 1946 the number of recorded cases was 155, but by 1953 the number had risen to 470. This jump in the figure accords with the observation that in one clinic 9 cases were discovered among 5,110 patients in one year, while in the previous 10 years only 8 were reported out of 44,870 examinations. Improvements in technique and increased awareness of the condition have rendered it more amenable to diagnosis.

The diagnosis of gastric diverticulum is made by the radiologist in 2/3 of the cases. Yet it is freely admitted that repeated barium-meal studies may miss the lesion. Reasons for this include the possibilities that the diverticulum may be filled with mucus or debris, or that the orifice may be too small to permit the entry of the barium. I would suggest that gastroscopy will assist considerably to reduce the number of missed cases.

Figures have shown that 75—80% of all gastric diverticula occur 3—5 cm. from the cardia on the posterior wall, 15% occur near the pylorus, and a small percentage are on the greater curvature. Therefore about 98% should be accessible to gastroscopic observation. Furthermore, the gastroscopic appearance of a diverticulum is frequently characteristic, and can be well contrasted with that of an ulcer. This is especially important in lesions near the pylorus, where serious pathological conditions tend to occur. It is not uncommon for these to produce defects which appear on the roentgenogram as sac-like defects, e.g. benign ulcer crater, perforating ulcer with accessory pocket formation, or gastric neoplasm with central necrosis. The consequences of misdiagnosis of a lesion in this area are so serious that it has been suggested that every case with a diverticulum in this area should have an operation. Here again it is apparent that gastroscopy may yield valuable information prior to surgery.

A further point which requires emphasis is the possibility of the presence of a double pathological condition in the upper alimentary tract. A gastric diverticulum may occasionally be responsible for the patient's symptoms, e.g. as a cause of haematemesis or perforation, but it would always be wise to seek some other explanation for a dyspeptic complaint. Thus 9 out of 21 cases in one series were found to have some other pathological condition as well, e.g. duodenal ulcer, gastric ulcer, or cholecystitis. In 6 of the 21 it was thought that the diverticulum was responsible for the symptoms. It is possible that even a higher percentage of cases may have been found to have an organic cause for the symptoms if gastroscopy had been undertaken, e.g. an atrophic gastric mucosa may well have been present. It is noteworthy that in one asymptomatic case a diverticulum was known to be present for 25 years.

It is apparent therefore that in this condition the combined efforts of the clinician, radiologist and gastroscopist are required in order to fully establish the diagnosis.

Victor Gorvy

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18 February 1955

* Price, E. A. (1955): S. Afr. Med. J., **29**, 153 (12 February).
Sommer, A. W. and Goodrich, W. A. (1953): J. Amer. Med. Assoc., **153**, 1424.